Comprehensive Guidelines for Prevention and Control of Dengue and Dengue Haemorrhagic Fever

Revised and expanded edition

World Health Organization
Regional Office for South-East Asia

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Preface

Dengue fever is the fastest emerging arboviral infection spread by *Aedes* mosquitoes with major public health consequences in over 100 tropical and sub-tropical countries in South-East Asia, the Western Pacific and South and Central America. Up to 2.5 billion people globally live under the threat of dengue fever and its severe forms—dengue haemorrhagic fever (DHF) or dengue shock syndrome (DSS). More than 75% of these people, or approximately 1.8 billion, live in the Asia-Pacific Region. As the disease spreads to new geographical areas, the frequency of the outbreaks is increasing along with a changing disease epidemiology. It is estimated that 50 million cases of dengue fever occur worldwide annually and half a million people suffering from DHF require hospitalization each year, a very large proportion of whom (approximately 90%) are children less than five years old. About 2.5% of those affected with dengue die of the disease.

Outbreaks of dengue fever in the 1950s and 1960s in many countries of the Asia-Pacific Region led to the organization of a biregional seminar in 1964 in Bangkok, Thailand, and a biregional meeting in 1974 in Manila, Philippines. Following these meetings, guidelines for the diagnosis, treatment and control of dengue fever were developed by the World Health Organization (WHO) in 1975. WHO has since then provided relentless support to its Member States by way of technical assistance, workshops and meetings, and issuing several publications. These include a set of revised guidelines in 1980, 1986 and 1995 following the research findings on pathophysiology and clinical and laboratory diagnosis. The salient features of the resolution of the Forty-sixth World Health Assembly (WHA) in 1993 urging the strengthening of national and local programmes for the prevention and control of dengue fever, DHF and DSS were also incorporated in these revised guidelines.

A global strategy on dengue fever and DHF was developed in 1995 and its implementation was bolstered in 1999. Subsequently, the awareness of variable responses to the infection presenting a complex epidemiology and demanding specific solutions necessitated the publication of the Comprehensive Guidelines for the Prevention and Control of Dengue/DHF with specific focus on the WHO South-East Asia Region in 1999. This document has served as a roadmap for Member States of the Region and elsewhere by providing guidance on the various challenges posed by dengue fever, DHF and DSS.

The 2002 World Health Assembly Resolution urged greater commitment to dengue from Member States and WHO. The International Health Regulations (2005) required Member States to detect and respond to any disease (including dengue) that demonstrates the ability to cause serious public health impact and spread rapidly globally. An Asia-Pacific Dengue Partnership was established

in 2007 to increase public and political commitment, to more effectively mobilize resources, and implement measures of prevention and control in accordance with the Global Strategy.

In 2008, a biregional (for the WHO South-East Asia and Western Pacific Regions) Asia-Pacific Dengue Strategic Plan (2008–2015) was developed to reverse the rising trend of dengue in the Member States of these regions. A voluminous quantity of research and studies conducted by WHO and other experts have additionally brought to light new developments and strategies in relation to case diagnosis and management of vector control, and emphasized regular sensitization and capacity-building. The publications underscored as well as reinforced the need for multisectoral partnerships in tandem with the revitalization of primary health care and transferring the responsibility, capability, and motivation for dengue control and prevention to the community, backed up by effective communication and social mobilization initiatives, for responsive behaviour en route to a sustainable solution of the dengue/DHF menace. This is important because dengue is primarily a man-made health problem attributed to globalization, rapid unplanned and unregulated development, deficient water supply and solid waste management with consequent water storage, and sanitary conditions that are frequently unsatisfactory leading to increasing breeding habitats of vector mosquitoes. All this, needless to say, necessitates a multidisciplinary approach.

In this edition of the ***Comprehensive Guidelines for the Prevention and Control of Dengue and Dengue Haemorrhagic Fever***, the contents have been extensively revised and expanded with the focus on new/additional topics of current relevance to Member States of the South-East Asia Region. Several case studies have been incorporated to illustrate best practices and innovations related to dengue prevention and control from various regions that should encourage replication subsequent to locale- and context-specific customization. In all, the *Guidelines* have 14 chapters that cover new insights into case diagnosis and management and details of surveillance (epidemiological and entomological), health regulations, vector bioecology, integrated vector management, the primary health care approach, communication for behavioural impact (COMBI), the Asia-Pacific Dengue Strategic Plan, case investigation, and emergency preparedness and outbreak response that has been previously published elsewhere by WHO and others.

This revised and expanded edition of the *Guidelines* is intended to provide guidance to national and local-level programme managers and public health officials as well as other stakeholders – including health practitioners, laboratory personnel and multisectoral partners – on strategic planning, implementation, and monitoring and evaluation towards strengthening the response to dengue prevention and control in Member States. The scientists and researchers involved in vaccine and antiviral drug development will also find crucial baseline information in this document.

It is envisioned that the wealth of information presented in this edition of the *Guidelines* will prove useful to effectively combat dengue fever, DHF and DSS in the WHO South-East Asia Region and elsewhere; and ultimately reduce the risk and burden of the disease.

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Abbreviations and Acronyms

ABCS	acidosis, bleeding, calcium, (blood) sugar
ADB	Asian Development Bank
Ae.	*Aedes*
AIDS	acquired immunodeficiency syndrome
ALT	alanine amino transferase
An.	Anopheles
APDP	Asia-Pacific Dengue Partnership
APDSP	Asia-Pacific Dengue Strategic Plan
APSED	Asia-Pacific Strategy for Emerging Diseases
AST	aspartate aminotransferase
BCC	behaviour change communication
BI	Breateau Index
BMA	Bangkok Municipal Administration
BP	blood pressure
Bs	*Bacillus sphaericus*
BSL2	Biosafety Level-2
Bt.H-14	*Bacillus thuringiensis* serotype H-14
BUN	blood urea nitrogen
CBC	complete blood count
CDC	Center for Disease Control, Atlanta, USA
CF	complement fixation
CFR	case-fatality rate
CI	Container Index
CNS	central nervous system
CPG	clinical practice guidelines
CPK	creatine-phosphokinase
CSF	cerebrospinal fluid
CT (or CAT)	computed axial tomography
Cx	Culex

COMBI	communication for behavioural impact
CPG	Clinical Practice Guidelines
CSR	corporate social responsibility
CSF	cerebrospinal fluid
CVP	central venous pressure
DALY	disability-adjusted lifeyear
DDT	dichlorodiphenyltrichloroethane
DEET	N, N-Diethyl-m-Toluamide
DENCO	Dengue and Control study (multicountry study)
DeVIT	Dengue Volunteer Inspection Team
DENV	dengue virus
DF	dengue fever
DHF	dengue haemorrhagic fever
DIC	disseminated intravascular coagulation
DNA	deoxyribonucleic acid
D/NSS	dextrose in isotonic normal saline solution
DLR	dextrose in lactated Ringer's solution
DSS	dengue shock syndrome
EAC	Emergency Action Committee
ECG	electrocardiography
EIP	extrinsic incubation period
ELISA	enzyme-linked immunosorbent assay
ENVID	European Network for Diagnostics of “Imported” Viral Diseases
ESR	erythrocyte sedimentation rate
G-6PD	glucose-6-phosphatase dehydrogenase
GIS	Geographical Information System
GPS	Global Positioning System
HCT	haematocrit
HE	health education
HFA	Health For All
HHT	hand-held terminal
HI	haemagglutination-inhibition
HI	House Index
HIA	Health Impact Assessment
HICDARM	hear, inform, convince, decision, action, reconfirmation, maintain
HIV	human immunodeficiency virus
ICP	intracranial pressure
IEC	information, education and communication
IFN-g	interferon gamma

IgG	immunoglobulin G
IgM	immunoglobulin M
IGR	insect growth regulator
IHR (2005)	International Health Regulations (2005)
IIFT	insecticide impregnated fabric trap
IPM	integrated pest management
ITN	insecticide-treated mosquito net
IRS	insecticide residual spraying
ISRE	intensive source reduction exercise
IV	intravenous
IVM	integrated vector management
KAP	knowledge, attitude, practice(s)
KABP	knowledge, attitude, belief, practice(s)
LAMP	loop-mediated amplification
LLIN	long-lasting insecticidal net
MAC-ELISA	IgM antibody-capture enzyme-linked immunosorbent assay
MDGs	Millennium Development Goals
M&E	monitoring and evaluation
MoH	Ministry of Health
mph	miles per hour
MRI	magnetic resonance imaging
M-RIP	massive, repetitive, intense, persistent
MS.CREFS	message, source, channel, receiver, effect, feedback, setting
NASBA	nucleic acid sequence-based amplification
NGO	nongovernmental organization
NS	nonstructural protein
NSAID	non-steroidal anti-inflammatory drugs
NK	natural killer cells
NS1	nonstructural protein 1
NT	neutralization test
OPD	outpatient department
ORS	oral rehyadration solution
PAHO	Pan American Health Organization
PCR	polymerase chain reaction
pH	potential hydrogen/presence of active hydrogen (hydrogen strength in a given substance to measure its acidity or alkalinity)
PHEIC	public health emergency of international concern
PHC	primary health care
PI	Pupal Index

ppm	parts per million
PRNT	plaque reduction neutralization test
PT	prothrombin time
PTT	partial thromboplastin time
R&D	research and development
RC	Regional Committee (of WHO SEA Region)
RDT	rapid diagnostic test
RNA	ribonucleic acid
RNAi	RNA interference
RR	relative risk
RS	remote sensing
RT-PCR	reverse transcriptase polymerase chain reaction
SEA	South-East Asia
SEARO	South-East Asia Regional Office (of WHO)
SMART	specific, measurable, appropriate, realistic, time-bound
TDR	tropical diseases research
TNF-a	tumor necrosis factor-a
TT	thrombin time/tourniquet test
ULV	ultra-low volume
UN	United Nations
UNEP	United Nations Environment Programme
UNICEF	United Nations Children's Fund
USAID	United States Agency for International Development
VHW	voluntary health worker
VPC	ventricular premature contraction
WBC	white blood cell
WHA	World Health Assembly
WHO	World Health Organization
WPRO	Regional Office for the Western Pacific (of WHO)

1. Introduction

Dengue fever (DF) and its severe forms—dengue haemorrhagic fever (DHF) and dengue shock syndrome (DSS)—have become major international public health concerns. Over the past three decades, there has been a dramatic global increase in the frequency of dengue fever (DF), DHF and DSS and their epidemics, with a concomitant increase in disease incidence (*Box 1*). Dengue is found in tropical and subtropical regions around the world, predominantly in urban and semi-urban areas. The disease is caused by a virus belonging to family *Flaviviradae* that is spread by *Aedes* (*Stegomyia*) mosquitoes. There is no specific treatment for dengue, but appropriate medical care frequently saves the lives of patients with the more serious dengue haemorrhagic fever. The most effective way to prevent dengue virus transmission is to combat the disease-carrying mosquitoes.

According to the *World Health Report 1996,*[1] the "re-emergence of infectious diseases is a warning that progress achieved so far towards global security in health and prosperity may be wasted". The report further indicated that: "infectious diseases range from those occurring in tropical areas (such as malaria and DHF, which are most common in developing countries) to diseases found worldwide (such as hepatitis and sexually transmitted diseases, including HIV/AIDS) and foodborne illnesses that affect large numbers of people in both the richer and poorer nations."

Box 1: Dengue and dengue haemorrhagic fever: Key facts

- Some 2.5 billion people – two fifths of the world's population in tropical and subtropical countries – are at risk.
- An estimated 50 million dengue infections occur worldwide annually.
- An estimated 500 000 people with DHF require hospitalization each year. A very large proportion (approximately 90%) of them are children aged less than five years, and about 2.5% of those affected die.
- Dengue and DHF is endemic in more than 100 countries in the WHO regions of Africa, the Americas, the Eastern Mediterranean, South-East Asia and the Western Pacific. The South-East Asia and Western Pacific regions are the most seriously affected.
- Epidemics of dengue are increasing in frequency. During epidemics, infection rates among those who have not been previously exposed to the virus are often 40% to 50% but can also reach 80% to 90%.
- Seasonal variation is observed.
- *Aedes (Stegomyia) aegypti* is the primary epidemic vector.
- Primarily an urban disease, dengue and DHF are now spreading to rural areas worldwide.
- Imported cases are common.
- Co-circulation of multiple serotypes/genotypes is evident.

The first confirmed epidemic of DHF was recorded in the Philippines in 1953–1954 and in Thailand in 1958. Since then, Member countries of the WHO South-East Asia (SEA) and Western Pacific (WP) regions have reported major dengue outbreaks at regular frequencies. In India, the

first confirmed DHF outbreak occurred in 1963. Other countries of the Region, namely Indonesia, Maldives, Myanmar and Sri Lanka, have also reported major DHF outbreaks. These outbreaks prompted a biregional (SEA and WP regions) meeting on dengue in 1974 in Manila, the Philippines, where technical guidelines for the diagnosis, treatment, and prevention and control of dengue and DHF were developed. This document was later revised at a summit meeting in Bangkok in 1980.

In May 1993, the Forty-sixth World Health Assembly (46th WHA, 1993) adopted a resolution on dengue prevention and control, which urged that the strengthening of national and local programmes for the prevention and control of dengue fever (DF), DHF and DSS should be among the foremost health priorities of those WHO Member States where the disease is endemic. The resolution also urged Member States to: (1) develop strategies to contain the spread and increasing incidence of dengue in a manner sustainable; (2) improve community health education; (3) encourage health promotion; (4) bolster research; (5) expand dengue surveillance; (6) provide guidance on vector control; and (7) prioritize the mobilization of external resources for disease prevention. In response to the World Health Assembly resolution, a global strategy for the operationalization of vector control was developed. It comprised five major components, as outlined in *Box 2*.

Box 2: Salient Features of Global Strategy for Control of DF/DHF Vectors

- Selective integrated mosquito control with community and intersectoral participation.
- Active disease surveillance based on strong health information systems.
- Emergency preparedness.
- Capacity-building and training.
- Intensive research on vector control.

Accordingly, several publications were issued by three regional offices of the World Health Organization—South-East Asia (SEARO) [*Monograph on dengue/dengue haemorrhagic fever* in 1993, a regional strategy for the control of DF/DHF in 1995, and *Guidelines on Management of Dengue Epidemics* in 1996]; Western Pacific (WPRO) [*Guidelines for Dengue Surveillance and Mosquito Control* in 1995]; and the Americas (AMRO PAHO) [*Dengue and Dengue Haemorrhagic Fever in the Americas: Guidelines for Prevention and Control* in 1994].

A 2002 World Health Assembly resolution (WHA 55.17) urged greater commitment to dengue from Member States and WHO. In 2005, the International Health Regulations (IHR) were formulated. These regulations stipulated that Member States detect and respond to any disease (for example, dengue) that has demonstrated the ability to cause serious public health impact and spread rapidly internationally.[2]

More recently, a biregional (SEA and WP regions) Asia-Pacific Dengue Strategic Plan (2008–2015) was developed to reverse the rising trend of dengue in the Member countries of these Regions. This has been endorsed by the Regional Committees of both the South-East Asia Region [resolution SEA/RC61/R5 (2008)] and the Western Pacific Region [resolution WPR/RC59/R6 (2008)].

Due to the high disease burden, dengue has become a priority area for several global organizations other than WHO, including the United Nations Children's Fund (UNICEF), United Nations Environment Programme (UNEP), the World Bank, and the WHO Special Programme for Research and Training in Tropical Diseases (TDR), among others.

In this backdrop, the 1999 Guidelines for Prevention and Control of Dengue/DHF (*WHO Regional Publication, SEARO No. 29*) have been revised, updated and rechristened as the "***Comprehensive Guidelines for Prevention and Control of Dengue and Dengue Haemmorhagic Fever: Revised and Expanded".*** These *Guidelines* incorporate new developments and strategies in dengue prevention and control.

2. Disease Burden of Dengue Fever and Dengue Haemorrhagic Fever

2.1 Global

Dengue epidemics are known to have occurred regularly over the last three centuries in tropical, subtropical and temperate areas around the world. The first epidemic of dengue was recorded in 1635[3] in the French West Indies, although a disease outbreak compatible with dengue had been reported in China as early as 992 AD.[4] During the 18th, 19th and early 20th centuries, epidemics of dengue-like diseases were reported and recorded globally, both in tropical as well as some temperate regions. Rush[5] was probably describing dengue when he wrote of "break-bone fever" occurring in Philadelphia in 1780. Most of the cases during the epidemics of that time mimicked clinical DF, although some displayed characteristics of the haemorrhagic form of the disease.

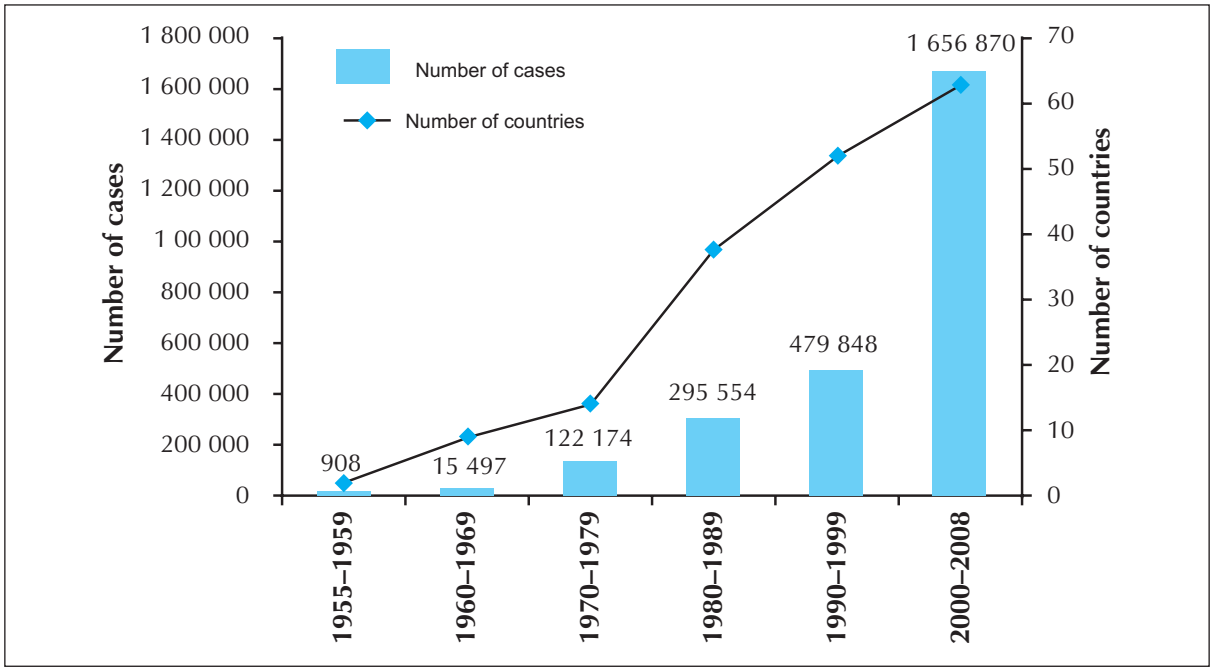
In most Central and South American countries, effective disease prevention was achieved by eliminating the principal epidemic mosquito vector, *Aedes aegypti*, during the 1950s and 1960s. In Asia, however, effective mosquito control was never achieved. A severe form of haemorrhagic fever, most likely akin to DHF, emerged in some Asian countries following World War II. From the 1950s through 1970s, this form of dengue was reported as epidemics periodically in a few Asian countries such as India, Philippines and Thailand.

During the 1980s, incidence increased markedly and distribution of the virus expanded to the Pacific islands and tropical America.[6] In the latter region, the species re-infested most tropical countries in the 1980s on account of disbanding of the *Ae. aegypti* eradication programme in the early 1970s. Increased disease transmission and frequency of epidemics were also the result of circulation of multiple serotypes in Asia. This brought about the emergence of DHF in the Pacific Islands, the Caribbean, and Central and South America. Thus, in less than 20 years by 1998, the American tropics and the Pacific Islands went from being free of dengue to having a serious dengue/DHF problem.[6]

Every 10 years, the average annual number of cases of DF/DHF cases reported to WHO continues to grow exponentially. From 2000 to 2008, the average annual number of cases was 1 656 870, or nearly three-and-a-half times the figure for 1990–1999, which was 479 848 cases (Figure 1). In 2008, a record 69 countries from the WHO regions of South-East Asia, Western Pacific and the Americas reported dengue activity.

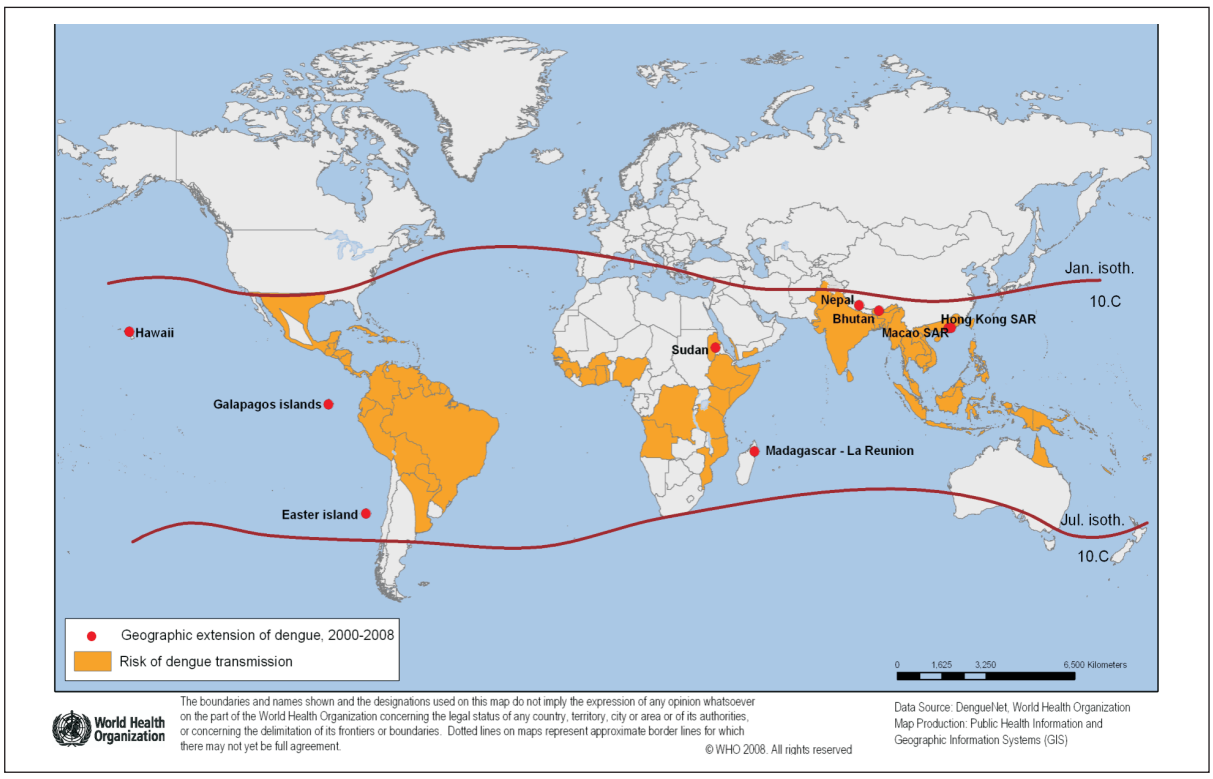
Geographical extension of the areas with dengue transmission or resurgent dengue activity has been documented in Bhutan, Nepal, Timor-Leste, Hawaii (USA), the Galapagos Islands (Ecuador), Easter Island (Chile), and the Hong Kong Special Administrative Region and Macao Special Administrative Region of China between 2001 and 2004 *(Figure 2)*. Nine outbreaks of dengue occurred in north Queensland, Australia, in four years from 2005 to 2008.[7]

Figure 1: Average annual number of cases of DF/DHF reported to WHO



Source: www.who.int.

Figure 2: Countries and areas at risk of dengue transmission, 2008



Source: Dengue Net, WHO, 2008. www.abc.net.au/rn/backgroundbriefing/documents/20100221_map.pdf

All four dengue viruses are circulating in Asia, Africa and the Americas. Due to early detection and better case management, reported case-fatality rates have been lower in recent years than in the decades before 2000.[8] Countries/areas at risk of dengue transmission in 2008 are shown in *Figure 2* and the major risk factors associated with DF/DHF are outlined in *Box 3*.

Box 3: Risk factors associated with DF/DHF

- *Demographic and societal changes:* Demographic and societal changes leading to unplanned and uncontrolled urbanization has put severe constraints on civic amenities, particularly water supply and solid waste disposal, thereby increasing the breeding potential of the vector species.
- *Water supply:* Insufficient and inadequate water distribution.
- *Solid waste management:* Insufficient waste collection and management.
- *Mosquito control infrastructure:* Lack of mosquito control infrastructure.
- *Consumerism:* Consumerism and introduction of non-biodegradable plastic products, paper cups, used tyres, etc. that facilitate increased breeding and passive spread of the disease to new areas (such as via the movement of incubating eggs because of the trade in used tyres).
- *Increased air travel and globalization of trade:* Increased air travel and globalization of trade has significantly contributed to the introduction of all the DENV serotypes to most population centres of the world.
- *Microevolution of viruses:*[9] The use of the most powerful molecular tools has revealed that each serotype has developed many genotypes as a result of microevolution. There is increasing evidence that virulent strains are replacing the existing non-virulent strains. Introduction of Asian DENV-2 into Cuba in 1981, which coincided with the appearance of DHF, is a classic example.

The burden of illness caused by dengue is measured by a set of epidemiological indicators such as the number of clinical cases classified by severity (DF, DHF, DSS), duration of illness episode, quality of life during the illness episode, case-fatality rate and absolute number of deaths during a given period of time. All these epidemiological indicators are combined into a single health indicator, such as disability-adjusted life years (DALYs).[a]

2.2 The WHO South-East Asia Region

Of the 2.5 billion people around the world living in dengue endemic countries and at risk of contracting DF/DHF, 1.3 billion live in 10 countries of the WHO South-East Asia (SEA) Region which are dengue endemic areas. Till 2003, only eight countries in the Region had reported dengue cases. By 2009, all Member countries except the Democratic People's Republic (DPR) of Korea reported dengue outbreaks. Timor-Leste reported an outbreak in 2004 for the first time. Bhutan also reported its first dengue outbreak in 2004.[10] Similarly, Nepal too reported its first indigenous case of dengue in November 2004.[11]

The reported dengue cases and deaths between 1985 and 2009 in 10 countries of the WHO SEA Region (all Member States except DPR Korea) (*Table 1 and Table 2*) underscore the public health importance of this disease in the Region.

The number of dengue cases has increased over the last three to five years, with recurring epidemics. Moreover, there has been an increase in the proportion of dengue cases with their severity, particularly in Thailand, Indonesia and Myanmar. The trends in reported cases and case-fatality rates are shown in *Figure 3*.

a Details with example are presented in chapter 14.

Table 1: Dengue cases reported from countries of the SEA Region, 1985–2009

Country	1985	1986	1987	1988	1989	1990	1991	1992	1993	1994	1995	1996	1997	"1998	"1999	2000	2001	2002	2003	2004	2005	2006	2007	2008	2009
Bangladesh	0	0	0	0	0	0	0	0	0	0	0	0	0	0	273	5 555	2 430	6 104	486	3 934	1 048	2 198	466	1 181	474
Bhutan	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	2 579	11	116	120	37	351
India	NA	NA	NA	N			6 291	2 683	11 125	7 494	7 847	16 517	1 177	707	944	650	3 306	1 926	12 754	4 153	11 985	12 317	5 023	11 476	15 535
Indonesia	13 588	16 529	23 864	44 573	10 362	22 807	21 120	17 620	17 418	18 783	35 102	44 650	30 730	72 133	21 134	33 443	45 904	40 377	51 934	79 462	95 279	106 425	157 442	155 607	156 052
Maldives	0	0	0	2 054	0	0	0	0	0	0	0	0	3	1 750	118	180	73	27	38	742	1 126	2 768	1 680	1 476	774
Myanmar	2 666	2 092	7 231	1 178	1 196	5 242	6 772	1 685	2 279	11 647	2 477	1 854	4 500	13 002	5 828	1 884	15 695	16 047	7 907	7 369	17 454	11 383	15 285	14 480	24 287
Nepal	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	25	3	6	30
Sri Lanka				10	203	1 350	1 048	656	750	582	440	1 298	980	1 275	1 688	3 343	4 304	8 931	4 749	15 463	5 994	11 980	7 314	6 555	35 010
Thailand	80 076	27 837	174 285	26 926	74 391	92 002	43 511	41 125	67 017	51 688	60 330	37 929	101 689	129 954	24 826	18 617	139 327	114 800	62 767	38 367	45 893	42 456	62 949	89 626	25 194
Timor-Leste																				434	1 128	162	227	108	175
SEA Region	96 330	46 458	205 380	74 741	86 152	121 401	78 742	63 769	98 589	90 194	106 196	102 248	139 079	218 821	54 811	63 672	211 039	188 212	140 635	152 503	179 918	189 830	250 509	280 552	232 530

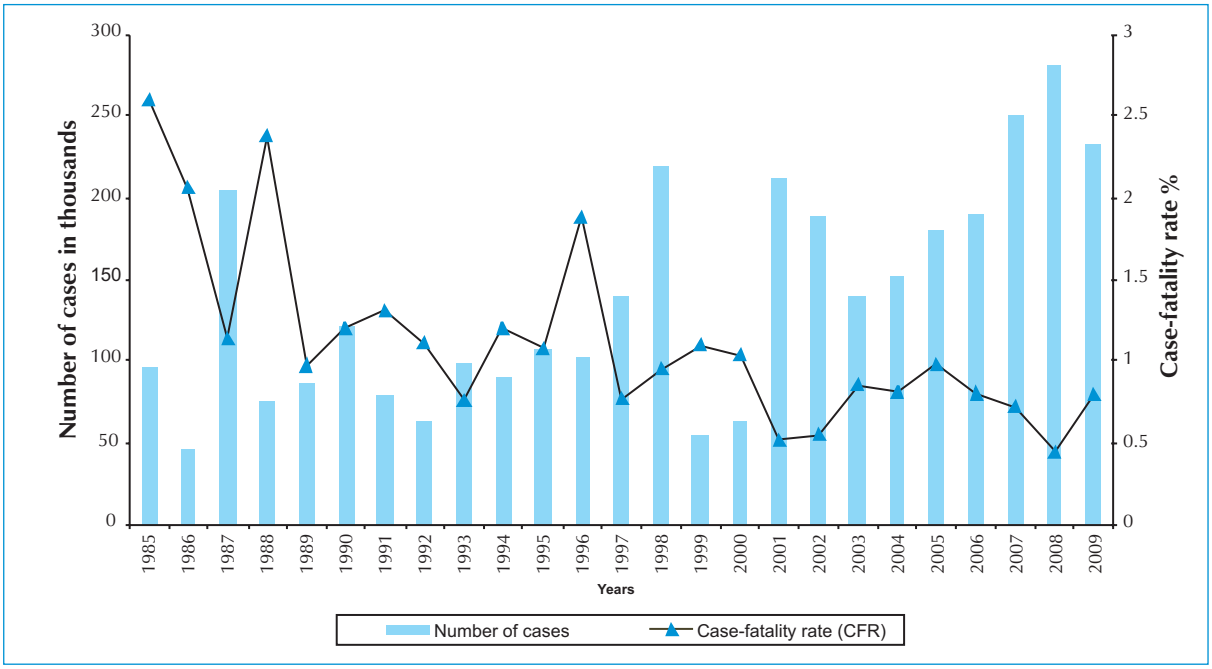
Source: WHO-SEARO, 2009.

Table 2: Dengue deaths and case-fatality rates (CFR) reported from countries of the SEA Region, 1985–2009

Country	1985	1986	1987	1988	1989	1990	1991	1992	1993	1994	1995	1996	1997	1998	1999	2000	2001	2002	2003	2004	2005	2006	2007	2008	2009
Bangladesh	0	0	0	0	0	0	0	0	0	0	0	0	0	0	4	93	44	58	10	13	4	11	1	0	0
Bhutan	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	5	3	8
India	NA	NA	NA	NA	NA	NA	3	12	36	4	10	545	36	18	17	7	53	33	215	45	157	184	62	79	96
Indonesia	460	608	1 105	1 527	464	821	578	509	418	471	885	1 192	681	1 414	422	472	497	533	794	957	1 298	1 096	1 446	940	1 396
Maldives	0	0	0	9	0	0	0	0	0	0	0	0	0	0	1	1	0	1	0	3	0	10	2	3	2
Myanmar	134	111	227	64	62	179	282	37	67	461	53	18	82	211	88	14	204	170	78	79	169	128	171	100	181
Nepal	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Sri Lanka	NA	NA	NA	0	20	54	31	15	7	7	11	54	17	8	14	37	54	64	32	88	27	44	25	19	346
Thailand	542	236	1 007	179	290	414	137	136	222	140	183	116	253	424	56	32	245	176	73	48	71	59	67	102	2
Timor-Leste																				2	40	0	6	1	0
SEA Region	1 136	955	2 339	1 779	836	1 468	1 031	709	750	1 083	142	1 925	1 069	2 075	602	656	1 097	1 035	1 202	1 235	1 766	1 532	1 785	1 247	2 031
Case-fatality rate	1.18	2.06	1.14	2.38	0.97	1.21	1.31	1.11	0.76	1.20	1.08	1.88	0.77	0.95	1.10	1.03	0.52	0.55	0.85	0.81	0.98	0.81	0.71	0.44	0.79

Source: WHO-SEARO, 2009.

Figure 3: Trends in reported number of dengue cases and case-fatality rates (CFR) reported from countries of the SEA Region, 1985–2009



Source: Country reports

The above figure shows that in countries of the SEA Region the trend of dengue cases is showing an increase over the years. The case-fatality rate (CFR), however, has registered a declining trend since 1985 and this could be attributed to better case management.

Variable endemicity for DF/DHF in countries of the SEA Region

DF/DHF is endemic in most countries of the SEA Region and detection of all four serotypes has now rendered these countries hyperendemic. However, the endemicity in Bhutan and Nepal is uncertain (*Box 4*).

Box 4: Variable endemicity of DF/DHF in countries of the SEA Region

Category A (Bangladesh, India, Indonesia, Maldives, Myanmar, Sri Lanka, Thailand and Timor-Leste)

- Major public health problem.
- Leading cause of hospitalization and death among children.
- Hyperendemicity with all four serotypes circulating in urban areas.
- Spreading to rural areas.

Category B (Bhutan, Nepal)

- Endemicity uncertain.
- Bhutan: First outbreak reported in 2004.
- Nepal: Reported first indigenous dengue case in 2004[11].

Category C (DPR Korea)

- No evidence of endemicity.

3. Epidemiology of Dengue Fever and Dengue Haemorrhagic Fever

The transmission of dengue virus depends upon biotic and abiotic factors. Biotic factors include the virus, the vector and the host. Abiotic factors include temperature, humidity and rainfall.

3.1 The virus

The dengue viruses are members of the genus *Flavivirus* and family *Flaviviridae*. These small (50 nm) viruses contain single-strand RNA as genome. The virion consists of a nucleocapsid with cubic symmetry enclosed in a lipoprotein envelope. The dengue virus genome is 11 644 nucleotides in length, and is composed of three structural protein genes encoding the nucleocaprid or core protein (C), a membrane-associated protein (M), an envelope protein (E), and seven non-structural protein (NS) genes. Among non-structural proteins, envelope glycoprotein, NS1, is of diagnostic and pathological importance. It is 45 kDa in size and associated with viral haemagglutination and neutralization activity.

The dengue viruses form a distinct complex within the genus *Flavivirus* based on antigenic and biological characteristics. There are four virus serotypes, which are designated as DENV-1, DENV-2, DENV-3 and DENV-4. Infection with any one serotype confers lifelong immunity to that virus serotype. Although all four serotypes are antigenically similar, they are different enough to elicit cross-protection for only a few months after infection by any one of them. Secondary infection with another serotype or multiple infections with different serotypes leads to severe form of dengue (DHF/DSS).

There exists considerable genetic variation within each serotype in the form of phylogenetically distinct "sub-types" or "genotypes". Currently, three sub-types can be identified for DENV-1, six for DENV-2 (one of which is found in non-human primates), four for DENV-3 and four for DENV-4, with another DENV-4 being exclusive to non-human primates.[12]

Dengue viruses of all four serotypes have been associated with epidemics of dengue fever (with or without DHF) with a varying degree of severity.

3.2 Vectors of dengue

Aedes (Stegomyia) aegypti (*Ae. aegypti)* and *Aedes (Stegomyia) albopictus* (*Ae. albopictus)* are the two most important vectors of dengue.[b]

b Further details on vectors are presented in Chapter 9.

Aedes (Stegomyia) aegypti

The *Aedes (Stegomyia) aegypti (Ae. aegypti)*[c] mosquito originates in Africa, where it exists as a feral species breeding in forests independent of humans. At a later stage, the species adapted to the peridomestic environment by breeding in water storage containers in the African region. Slave trade and commerce with the rest of the world in the 17th to 19th centuries provided a mechanism for the species to be introduced to the "New World" and South-East Asia.[4] By 1800, the species had entrenched itself in many large tropical coastal cities around the world.

World War II provided yet another opportunity to the species for penetration into inland areas through the increased navigation into the hinterland by country boats on river systems. Increased transport, human contact, urbanization and the proliferation of drinking water supply schemes in rural areas ultimately led to the species getting entrenched in both urban and rural areas of most parts of the world. On account of the species' high degree of domestication and strong affinity for human blood, it achieved high vectorial capacity for transmission of DF/DHF in all the areas where it prevailed. As per the distribution related records, *Ae. aegypti* now persists in most of the countries, and even in those from where it had been eradicated. Today, *Ae. aegypti* is a cosmotropical species[13] between latitudes 45°N and 35°S.

Aedes (Stegomyia) albopictus

Aedes (Stegomyia) albopictus[d] belongs to the *scutellaris* group of subgenus *Stegomyia*. It is an Asian species indigenous to South-East Asia and islands of the Western Pacific and the Indian Ocean. However, during the last few decades the species has spread to Africa, West Asia, Europe and the Americas (North and South) after extending its range eastward to the Pacific islands during the early 20th century.

The majority of the introductions are passive due to transportation of dormant eggs through international shipments of used tyres. In newly infested countries and those threatened with introduction, there has been considerable concern that *Ae. albopictus* would cause serious outbreaks of arboviral diseases since *Ae. albopictus* is a competent vector of at least 22 arboviruses, notably dengue (all four serotypes), which is more commonly transmitted by *Ae. aegypti*.[14]

Figures 4a and *4b* show the global distribution of *Ae. aegypti* and *Ae. albopictus*.[15]

c The subgenus *Stegomyia* has been upgraded to genus level, known as *Stegomyia aegypti*. However, for simplicity of reference, the name has been retained as *Ae. aegypti* [Reinert J.F. et al. Phylogeny and Classification of Aedine *(Diptera: Culicidae),* based on morphological characters of all life stages. Zoo. Jr. Linnean Society, 2004; Polaszek. A. Two words colliding: Resistance to changes in the scientific names of animals—Aedes versus Stegomyia. Trends Parasital, 2006, 22 (1): 8-9; *Jr.Med. Entom*. Policy on Names of Aedine Mosquito Genre and Subgenre].

d The sub-genus, *Stegomyia* has been upgraded to genus level, called as *Stegomyia albopictus*. However for simplicity of reference, the name has been retained as *Ae. albopictus* (Reinert J.F. et al. Phylogeny and classification of Aedine (Diptera: Culicidae), based on morphological characters of all life stages. Zoo. Jr. Linnean Society, 2004; Polaszek. A. Two words colliding: resistance to changes in the scientific names of animals--Aedes versus Stegomyia. Trends Parasital, 2006, 22 (1): 8-9; *Jr.Med. Entom*. Policy on Names of Aedine Mosquito Genre and Sub-genre).

Figure 4a: Global distribution of *Ae. aegypti*

Source: Rogers D.J., Wilson, A.J., Hay, S.L. The global distribution of yellow fever and dengue. *Adv. Parasitol. 2006. 62:181–220.*[15]

Figure 4b: Global distribution of *Ae. albopictus*

Source: Rogers D.J., Wilson, A.J., Hay, S.L. The global distribution of yellow fever and dengue. *Adv. Parasitol. 2006. 62:181–220.*[15]

Vectorial competency and vectorial capacity

The terminology of vectorial competency and vectorial capacity has been used interchangeably in literature. Recently, however, these have been defined.

Vectorial competency

Vectorial competency denotes:

- High susceptibility to infecting virus.
- Ability to replicate the virus.
- Ability to transmit the virus to another host.

Both *Ae. aegypti* and *Ae. albopictus* carry high vectorial competency for dengue viruses.

Vectorial capacity

Vectorial capacity is governed by the environmental and biological characteristics of the species, and thus these two species differ in their vectorial capacity.

Ae. aegypti is a highly domesticated, strongly anthropophilic, nervous feeder (i.e. it bites more than one host to complete one blood meal) and is a discordant species (i.e. it needs more than one feed for the completion of the gonotropic cycle). These habits epidemiologically result in the generation of multiple cases and the clustering of dengue cases in cities. On the contrary, *Ae. albopictus* still maintains feral moorings and partly invades peripheral areas of urban cities, and thus feeds on both humans and animals. It is an aggressive feeder and a concordant species, i.e. the species can complete its blood meal in one go on one person and also does not require a second blood meal for the completion of the gonotropic cycle. Hence, *Ae. albopictus* carries poor vectorial capacity in an urban epidemic cycle.

3.3 Host

Dengue viruses, having evolved from mosquitoes, adapted to non-human primates and later to humans in an evolutionary process. The viraemia among humans builds up high titres two days before the onset of the fever (non-febrile) and lasts 5–7 days after the onset of the fever (febrile). It is only during these two periods that the vector species gets infected. Thereafter, the humans become dead-ends for transmission. The spread of infection occurs through the movement of the host (man) as the vectors' movements are very restricted.

The susceptibility of the human depends upon the immune status and genetic predisposition.[16,17,18] Both monkeys and humans are amplifying hosts and the virus is maintained by mosquitoes transovarially via eggs.

3.4 Transmission of dengue virus

Transmission of dengue viruses occur in three cycles:

(1) ***Enzootic cycle***: A primitive sylvatic cycle maintained by monkey-*Aedes*-monkey cycle as reported from South Asia and Africa. Viruses are not pathogenic to monkeys and viraemia lasts 2–3 days.[19] All the four dengue serotypes (DENV-1 to -4) have been isolated from monkeys.

(2) ***Epizootic cycle***: The dengue virus crosses over to non-human primates from adjoining human epidemic cycles by bridge vectors. In Sri Lanka, the epizootic cycle was observed among touqe macaques (*Macaca sinica*) during 1986–1987 in a study area on a serological basis. Within the study area (three kilometres), 94% macaques were found affected.[20]

(3) ***Epidemic cycle***: The epidemic cycle is maintained by human-*Aedes aegypti*-human cycle with periodic/cyclical epidemics. Generally, all serotypes circulate and give rise to hyperendemicity. *Ae. aegypti* has generally low susceptibility to oral infection but its strong anthrophily with multiple feeding behaviour and highly domesticated habitats makes it an efficient vector. The persistence of dengue virus, therefore, depends on the development of high viral titres in the human host to ensure transmission in mosquitoes.[21]

Transmission of DF/DHF

For transmission to occur the female *Ae. aegypti* must bite an infected human during the viraemic phase of the illness that manifests two days before the onset of fever and lasts 4–5 days after onset of fever. After ingestion of the infected blood meal the virus replicates in the epithelial cell lining of

the midgut and escapes into haemocoele to infect the salivary glands and finally enters the saliva causing infection during probing. The genital track is also infected and the virus may enter the fully developed eggs at the time of oviposition. The extrinsic incubation period (EIP) lasts from 8 to 12 days and the mosquito remains infected for the rest of its life. The intrinsic incubation period covers five to seven days.[22]

Seasonality and intensity of transmission

Dengue transmission usually occurs during the rainy season when the temperature and humidity are conducive for build-up of the vector population breeding in secondary habitats as well as for longer mosquito survival.

In arid zones where rainfall is scanty during the dry season, high vector population builds up in man-made storage containers.

Ambient temperature, besides hastening the life-cycle of *Ae. aegypti* and resulting in the production of small-size mosquitoes, also reduces the extrinsic incubation period of the virus as well. Small-size females are forced to take more blood meals to obtain the protein needed for egg production. This has the effect of increasing the number of infected individuals and hastening the build-up of the epidemic[22] during the dry season.

A number of factors that contribute to initiation and maintenance of an epidemic include: (i) the strain of the virus, which may influence the magnitude and duration of the viraemia in humans; (ii) the density, behaviour and vectorial capacity of the vector population; (iii) the susceptibility of the human population (both genetic factors and pre-existing immune profile); and (iv) the introduction of the virus into a receptive community.[21]

Features of dengue viral infection in the community

DF/DHF syndrome

DF/DHF is characterized by the "iceberg" or pyramid phenomenon. At the base of the pyramid, most of the cases are symptomless, followed by DF, DHF and DSS. Clusters of cases have been reported in particular households or neighbourhoods due to the feeding behaviour of the vector.[23]

Affected population

The population affected varies from one outbreak to another. Actual estimates can be made by obtaining clinical/subclinical ratios during epidemics. In a well-defined epidemic study in North Queensland, Australia, with primary infection, 20% to 50% of the population was found affected.[24]

Severity of the disease

The serotype that produces the secondary infection and, in particular, the serotype sequence are important to ascertain the severity of the disease. All the four serotypes are able to produce DHF cases. However, during sequential infections, only 2% to 4% of individuals develop severe disease.[25]

Studies in Thailand have revealed that the DENV-1/DENV-2 sequence of infection was associated with a 500-fold risk of DHF compared with primary infection. For the DENV-3/DENV-2 sequence the risk was 150-fold, and a DENV-4/DENV-2 sequence had a 50-fold risk of DHF.[26]

There is no time-limit to sensitization after a primary infection. The 1997 Santiago de Cuba epidemic clearly demonstrated that with the introduction of DENV-2, DHF had occurred 16–20 years after the primary infection with DENV-1.[27]

Transmission sites

Due to the limited flight range of *Ae. aegypti,*[13] DF/DHF spread is caused by human movement. Receptivity (high-breeding potential for *Ae. aegypti*) and vulnerability (high potential for importation of virus) need to be mapped. Any congregation at receptive areas will result in either transmission from infected mosquito to human or from viraemic human to the uninfected mosquito. Hospitals, schools, religious institutions and entertainment centres where people congregate become the foci of transmission on account of high receptivity and vulnerability for DF/DHF. Further human movement spreads the infection to larger parts of the city.[28]

3.5 Climate change and its impact on dengue disease burden

Global climate change refers to large-scale changes in climate patterns over the years, including fluctuations in both rainfall- and temperature-related greenhouse effects (including the emission of carbon dioxide from burning fossil fuel and methane from paddy fields and livestock), whereby solar radiation gets trapped beneath the atmosphere. Global warming is predicted to lead to a 2.0 °C–4.5 °C rise in average global temperatures by the year 2100,[29] and this could have a perceptible impact on vector-borne diseases.[30]

The maximum impact of climate change on transmission is likely to be observed at the extreme end of the temperature range at which the transmission occurs. The temperature range for dengue fever lies between 14 °C and 18 °C at the lower end and 35 °C and 40 °C at the upper end. Although the vector species, being a domestic breeder, is endophagic and endophilic, it largely remains insulated by fitting into human ecological requirements. However, with a 2 °C increase in temperature the extrinsic incubation period of DENV will be shortened and more infected mosquitoes will be available for a longer period of time.[31] Besides that, mosquitoes will bite more frequently because of dehydration and thus further increase man-mosquito contact.

3.6 Other factors for increased risk of vector breeding

Other factors that facilitate increased transmission are briefly outlined below:

Urbanization

As per United Nations reports, 40% of the population in developing countries now lives in urban areas, which is projected to rise to 56% by 2030[e] largely due to rural–urban migration. Such migration from rural to urban areas is due to both "push" (seeking better earning avenues) and "pull" (seeking better amenities such as education, health care, etc.) factors. The failure of urban local governments to provide matching civic amenities and infrastructure to accommodate the influx generates unplanned settlements with inadequate potable water, poor sanitation including solid waste disposal, and poor public health infrastructure. All this raises the potential for *Ae. aegypti* breeding to a high level and makes the environment for transmission conducive.

e UN Population Division. *World Urbanization Prospects: The 2001 revision*. 2002. New York, UN. p.182. http://info.k4health.org/pr/m16/m16chap1_1.shtml

Increased global travel

With expanding travel and an exponential increase in tourism and trade, there exists a high possibility of introduction of new DENV serotypes/genotypes through healthy viraemic persons, thus helping in the build-up of a high transmission potential.

3.7 Geographical spread of dengue vectors

Ae. albopictus has spread farther north compared with *Ae. aegypti* (Figures 4a and 4b). Its eggs are somewhat resistant to sub-freezing temperatures.[32] This raises the possibility that *Ae. albopictus* could mediate a re-emergence of dengue in the United States of America or in Europe. This species survived the extreme winters in Italy[33] and was recently implicated in an outbreak of chikungunya in Italy.[34]

3.8 Future projections of dengue estimated through empirical models

Mathematical models project a substantial increase in the transmission of vector-borne diseases in various climate change situations. However, these models have been criticized on the grounds that they do not adequately account for rainfall, interaction between climate variables or relevant socioeconomic factors. The dengue vector *Ae. aegypti* is highly domesticated and breeds in safe clean waters devoid of any parasite, pathogen or predators. Similarly, adults feed on humans inside houses and rest in sequestered, dark places to complete the gonotropic cycles. In view of these ecological features, *Ae. aegypti* is least affected by climatic changes and instead maintains a high transmission potential throughout.

In an empirical model[35] vapour pressure – which is a measure of humidity – was incorporated to estimate the global distribution of dengue fever. It was concluded that the current geographical limits of dengue fever transmission can be modelled with 89% accuracy on the basis of long-term average vapour pressure. In 1990, almost 30% of the world population, i.e. 1.5 billion people, lived in regions where the estimated risk of dengue transmission was greater than 50%.

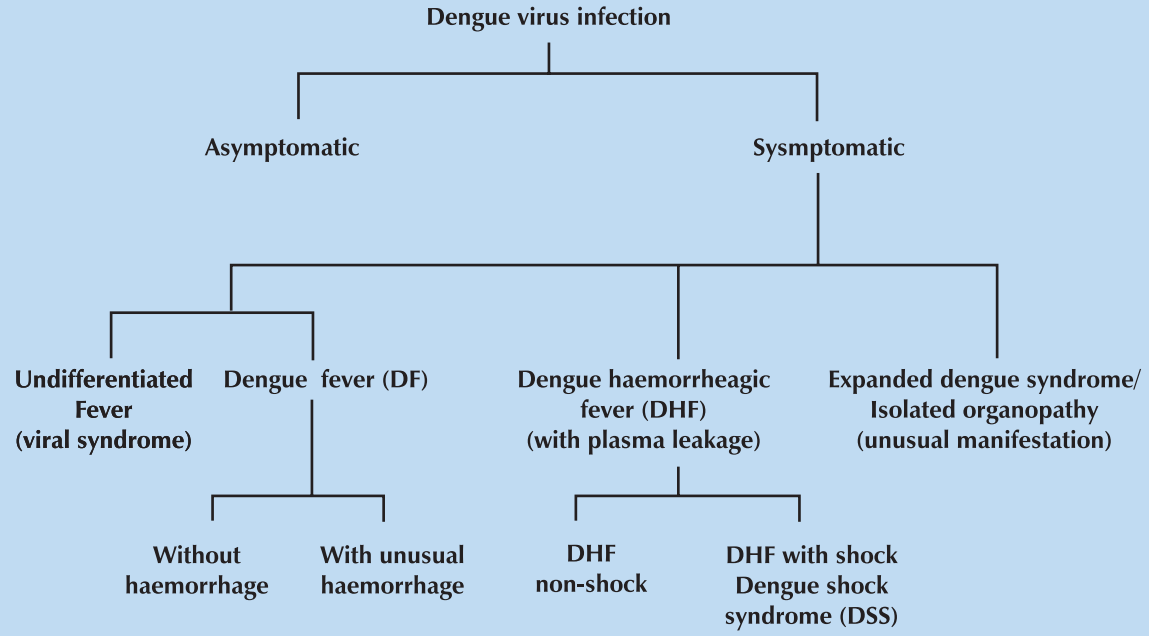
By 2085, given the population and climatic change projections, it is estimated that 5–6 billion people (50%–60% of the projected global population) would be at risk of dengue transmission compared with 3.5 billion people or 35% of the projected population if climate change would not set in. However, further research on this is needed.

4. Clinical Manifestations and Diagnosis[f]

4.1 Clinical manifestations

Dengue virus infection may be asymptomatic or may cause undifferentiated febrile illness (viral syndrome), dengue fever (DF), or dengue haemorrhagic fever (DHF) including dengue shock syndrome (DSS). Infection with one dengue serotype gives lifelong immunity to that particular serotype, but there is only short-term cross-protection for the other serotypes. The clinical manifestation depends on the virus strain and host factors such as age, immune status, etc. *(Box 5)*.

Box 5: Manifestations of dengue virus infection



The details of dengue virus infection are presented below.

Undifferentiated fever

Infants, children and adults who have been infected with dengue virus, especially for the first time (i.e. primary dengue infection), may develop a simple fever indistinguishable from other viral

f This chapter was reviewed at the Consultative Meeting on Dengue Case Classification and Case Management held in Bangkok, Thailand, on 7-8 October 2010. The participants included experts from SEARO and WPRO Member States and one observer each from the University of Massachusetts Medical School, USA, and Armed Forces Research Institute of Medical Sciences, Thailand, and the secretariat comprised members of the WHO Collaborating Centre for Case Management of Dengue/DHF/DSS, QSNICH (Bangkok, Thailand).

infections. Maculopapular rashes may accompany the fever or may appear during defervescence. Upper respiratory and gastrointestinal symptoms are common.

Dengue fever

Dengue fever (DF) is most common in older children, adolescents and adults. It is generally an acute febrile illness, and sometimes biphasic fever with severe headache, myalgias, arthralgias, rashes, leucopenia and thrombocytopenia may also be observed. Although DF may be benign, it could be an incapacitating disease with severe headache, muscle and joint and bone pains (break-bone fever), particularly in adults. Occasionally unusual haemorrhage such as gastrointestinal bleeding, hypermenorrhea and massive epistaxis occur. In dengue endemic areas, outbreaks of DF seldom occur among local people.

Dengue haemorrhagic fever

Dengue haemorrhagic fever (DHF) is more common in children less than 15 years of age in hyperendemic areas, in association with repeated dengue infections. However, the incidence of DHF in adults is increasing. DHF is characterized by the acute onset of high fever and is associated with signs and symptoms similar to DF in the early febrile phase. There are common haemorrhagic diatheses such as positive tourniquet test (TT), petechiae, easy bruising and/or GI haemorrhage in severe cases. By the end of the febrile phase, there is a tendency to develop hypovolemic shock (dengue shock syndrome) due to plasma leakage.

The presence of preceding warning signs such as persistent vomiting, abdominal pain, lethargy or restlessness, or irritability and oliguria are important for intervention to prevent shock. Abnormal haemostasis and plasma leakage are the main pathophysiological hallmarks of DHF. Thrombocytopenia and rising haematocrit/haemoconcentration are constant findings before the subsidence of fever/onset of shock. DHF occurs most commonly in children with secondary dengue infection. It has also been documented in primary infections with DENV-1 and DENV-3 as well as in infants.

Expanded dengue syndrome

Unusual manifestations of patients with severe organ involvement such as liver, kidneys, brain or heart associated with dengue infection have been increasingly reported in DHF and also in dengue patients who do not have evidence of plasma leakage. These unusual manifestations may be associated with coinfections, comorbidities or complications of prolonged shock. Exhaustive investigations should be done in these cases.

Most DHF patients who have unusual manifestations are the result of prolonged shock with organ failure or patients with comorbidities or coinfections.

4.2 Clinical features

Dengue fever

After an average intrinsic incubation period of 4–6 days (range 3–14 days), various non-specific, constitutional symptoms and headache, backache and general malaise may develop. Typically, the onset of DF is sudden with a sharp rise in temperature and is frequently associated with a flushed face[36] and headache. Occasionally, chills accompany the sudden rise in temperature. Thereafter, there may be retro-orbital pain on eye movement or eye pressure, photophobia, backache, and pain in the muscles and joints/bones. The other common symptoms include anorexia and altered

taste sensation, constipation, colicky pain and abdominal tenderness, dragging pains in the inguinal region, sore throat and general depression. These symptoms usually persist from several days to a few weeks. It is noteworthy that these symptoms and signs of DF vary markedly in frequency and severity.

Fever: The body temperature is usually between 39 °C and 40 °C, and the fever may be biphasic, lasting 5–7 days in the majority of cases.

Rash: Diffuse flushing or fleeting eruptions may be observed on the face, neck and chest during the first two to three days, and a conspicuous rash that may be maculopapular or rubelliform appears on approximately the third or fourth day. Towards the end of the febrile period or immediately after defervescence, the generalized rash fades and localized clusters of petechiae may appear over the dorsum of the feet, on the legs, and on the hands and arms. This convalescent rash is characterized by confluent petechiae surrounding scattered pale, round areas of normal skin. Skin itching may be observed.

Haemorrhagic manifestations: Skin haemorrhage may be present as a positive tourniquet test and/or petechiae. Other bleeding such as massive epistaxis, hypermenorrhea and gastrointestinal bleeding rarely occur in DF, complicated with thrombocytopenia.

Course: The relative duration and severity of DF illness varies between individuals in a given epidemic, as well as from one epidemic to another. Convalescence may be short and uneventful but may also often be prolonged. In adults, it sometimes lasts for several weeks and may be accompanied by pronounced asthenia and depression. Bradycardia is common during convalescene. Haemorrhagic complications, such as epistaxis, gingival bleeding, gastrointestinal bleeding, haematuria and hypermenorrhoea, are unusual in DF. Although rare, such severe bleeding (DF with unusual haemorrhage) are an important cause of death in DF.

Dengue fever with haemorrhagic manifestations must be differentiated from dengue haemorrhagic fever.

Clinical laboratory findings

In dengue endemic areas, positive tourniquet test and leukopenia (WBC ≤5000 cells/mm3) help in making early diagnosis of dengue infection with a positive predictive value of 70%–80%.[37,38]

The laboratory findings during an acute DF episode of illness are as follows:

- Total WBC is usually normal at the onset of fever; then leucopenia develops with decreasing neutrophils and lasts throughout the febrile period.
- Platelet counts are usually normal, as are other components of the blood clotting mechanism. Mild thrombocytopenia (100 000 to 150 000 cells/mm^3) is common and about half of all DF patients have platelet count below 100 000 cells/mm^3; but severe thrombocytopenia (<50 000 cells/mm^3) is rare.[39]
- Mild haematocrit rise (≈10%) may be found as a consequence of dehydration associated with high fever, vomiting, anorexia and poor oral intake.
- Serum biochemistry is usually normal but liver enzymes and aspartate amino transferase (AST) levels may be elevated.
- It should be noted that the use of medications such as analgesics, antipyretics, anti-emetics and antibiotics can interfere with liver function and blood clotting.

Differential diagnosis

The differential diagnoses of DF include a wide variety of diseases prevalent in the locality *(Box 6)*.

Box 6: Differential diagnoses of dengue[40]

- **Arboviruses:** Chikungunya virus (this has often been mistaken for dengue in South-East Asia).
- **Other viral diseases:** Measles; rubella and other viral exanthems; Epstein-Barr Virus (EBV); enteroviruses; influenza; hepatitis A; Hantavirus.
- **Bacterial diseases:** Meningococcaemia, leptospirosis, typhoid, melioidosis, rickettsial diseases, scarlet fever.
- **Parasitic diseases:** Malaria.

Dengue haemorrhagic fever and dengue shock syndrome

Typical cases of DHF are characterized by high fever, haemorrhagic phenomena, hepatomegaly, and often circulatory disturbance and shock[36,41]. Moderate to marked thrombocytopenia with concurrent haemoconcentration/rising haematocrit are constant and distinctive laboratory findings are seen. The major pathophysiological changes that determine the severity of DHF and differentiate it from DF and other viral haemorrhagic fevers are abnormal haemostasis and leakage of plasma selectively in pleural and abdominal cavities.

The clinical course of DHF begins with a sudden rise in temperature accompanied by facial flush and other symptoms resembling dengue fever, such as anorexia, vomiting, headache, and muscle or joint pains (Table 3)[41]. Some DHF patients complain of sore throat and an injected pharynx may be found on examination. Epigastric discomfort, tenderness at the right sub-costal margin, and generalized abdominal pain are common. The temperature is typically high and in most cases continues as such for 2–7 days before falling to a normal or subnormal level. Occasionally the temperature may be as high as 40 °C, and febrile convulsions may occur. A bi-phasic fever pattern may be observed.

Table 3: Non-specific constitutional symptoms observed in haemorrhagic fever patients with dengue and chikungunya virus infection

Symptom	DHF (%)	Chikungunya fever (%)
Injected pharynx	98.9	90.3
Vomiting	57.9	59.4
Constipation	53.3	40.0
Abdominal pain	50.0	31.6
Headache	44.6	68.4
Generalized lymphadenopathy	40.5	30.8
Conjunctival injection	32.8[a]	55.6[a]
Cough	21.5	23.3
Restlessness	21.5	33.3
Rhinitis	12.8	6.5
Maculopapular rash	12.1[a]	59.6[a]
Myalgia/arthralgia	12.0[a]	40.0[a]
Enanthema	8.3	11.1
Abnormal reflex	6.7	0.0
Diarrhoea	6.4	15.6
Palpable spleen (in infants of <6 months)	6.3	3.1
Coma	3.0	0.0

Source: Nimmannitya S., et al., *American Journal of Tropical Medicine and Hygiene,* 1969, 18:954-971.[41]
[a] Statistically significant difference.

A positive tourniquet test (≥10 spots/square inch), the most common haemorrhagic phenomenon, could be observed in the early febrile phase. Easy bruising and bleeding at venipuncture sites are present in most cases. Fine petechiae scattered on the extremities, axillae, and face and soft palate may be seen during the early febrile phase. A confluent petechial rash with small, round areas of normal skin is seen in convalescence, as in dengue fever. A maculopapular or rubelliform rash may be observed early or late in the disease. Epistaxis and gum bleeding are less common. Mild gastrointestinal haemorrhage is occasionally observed, however, this could be severe in pre-existing peptic ulcer disease. Haematuria is rare.

The liver is usually palpable early in the febrile phase, varying from just palpable to 2–4 cm below the right 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. It should be noted that the incidence of hepatomegaly is observer dependent. Splenomegaly has been observed in infants under twelve months and by radiology examination. A lateral decubitus chest X-ray demonstrating pleural effusion, mostly on the right side, is a constant finding. The extent of pleural effusion is positively correlated with disease severity. Ultrasound could be used to detect pleural effusion and ascites. Gall bladder oedema has been found to precede plasma leakage.

The critical phase of DHF, i.e. the period of plasma leakage, begins around the transition from the febrile to the afebrile phase. Evidence of plasma leakage, pleural effusion and ascites may, however, not be detectable by physical examination in the early phase of plasma leakage or mild cases of DHF. A rising haematocrit, e.g. 10% to 15% above baseline, is the earliest evidence.

Significant loss of plasma leads to hypovolemic shock. Even in these shock cases, prior to intravenous fluid therapy, pleural effusion and ascites may not be detected clinically. Plasma leakage will be detected as the disease progresses or after fluid therapy. Radiographic and ultrasound evidence of plasma leakage precedes clinical detection. A right lateral decubitus chest radiograph increases the sensitivity to detect pleural effusion. Gall bladder wall oedema is associated with plasma leakage and may precede the clinical detection. A significantly decreased serum albumin >0.5 gm/dl from baseline or <3.5 gm% is indirect evidence of plasma leakage.[39]

In mild cases of DHF, all signs and symptoms abate after the fever subsides. Fever lysis may be accompanied by sweating and mild changes in pulse rate and blood pressure. These changes reflect mild and transient circulatory disturbances as a result of mild degrees of plasma leakage. Patients usually recover either spontaneously or after fluid and electrolyte therapy.

In moderate to severe cases, the patient's condition deteriorates a few days after the onset of fever. There are warning signs such as persistent vomiting, abdominal pain, refusal of oral intake, lethargy or restlessness or irritability, postural hypotension and oliguria.

Near the end of the febrile phase, by the time or shortly after the temperature drops or between 3–7 days after the fever onset, there are signs of circulatory failure: the skin becomes cool, blotchy and congested, circum-oral cyanosis is frequently observed, and the pulse becomes weak and rapid. Although some patients may appear lethargic, usually they become restless and then rapidly go into a critical stage of shock. Acute abdominal pain is a frequent complaint before the onset of shock.

The shock is characterized by a rapid and weak pulse with narrowing of the pulse pressure ≤20 mmHg with an increased diastolic pressure, e.g. 100/90 mmHg, or hypotension. Signs of reduced tissue perfusion are: delayed capillary refill (>3 seconds), cold clammy skin and restlessness. Patients in shock are in danger of dying if no prompt and appropriate treatment is given. Patients may pass into a stage of profound shock with blood pressure and/or pulse becoming imperceptible (Grade 4 DHF). It is noteworthy that most patients remain conscious almost to the terminal stage. Shock is reversible and of short duration if timely and adequate treatment with volume-replacement is given.

Without treatment, the patient may die within 12 to 24 hours. Patients with prolonged or uncorrected shock may give rise to a more complicated course with metabolic acidosis and electrolyte imbalance, multiorgan failure and severe bleeding from various organs. Hepatic and renal failure are commonly observed in prolonged shock. Encephalopathy may occur in association with multiorgan failure, metabolic and electrolyte disturbances. Intracranial haemorrhage is rare and may be a late event. Patients with prolonged or uncorrected shock have a poor prognosis and high mortality.

Convalescence in DHF

Diuresis and the return of appetite are signs of recovery and are indications to stop volume replacement. Common findings in convalescence include sinus bradycardia or arrhythmia and the characteristic dengue confluent petechial rash as described for dengue fever. Convalescence in patients with or without shock is usually short and uneventful. Even in cases with profound shock, once the shock is overcome with proper treatment the surviving patients recover within 2 – 3 days. However, those who have prolonged shock and multiorgan failure will require specific treatment and experience a longer convalescence. It should be noted that the mortality in this group would be high even with specific treatment.

4.3 Pathogenesis and pathophysiology

DHF occurs in a small proportion of dengue patients. Although DHF may occur in patients experiencing dengue virus infection for the first time, most DHF cases occur in patients with a secondary infection.[42,43] The association between occurrence of DHF/DSS and secondary dengue infections implicates the immune system in the pathogenesis of DHF. Both the innate immunity such as the complement system and NK cells as well as the adaptive immunity including humoral and cell-mediated immunity are involved in this process.[44,45] Enhancement of immune activation, particularly during a secondary infection, leads to exaggerated cytokine response resulting in changes in vascular permeability. In addition, viral products such as NS1 may play a role in regulating complement activation and vascular permeability.[46,47,48]

The hallmark of DHF is the increased vascular permeability resulting in plasma leakage, contracted intravascular volume, and shock in severe cases. The leakage is unique in that there is selective leakage of plasma in the pleural and peritoneal cavities and the period of leakage is short (24–48 hours). Rapid recovery of shock without sequelae and the absence of inflammation in the pleura and peritoneum indicate functional changes in vascular integrity rather than structural damage of the endothelium as the underlying mechanism.

Various cytokines with permeability enhancing effect have been implicated in the pathogenesis of DHF.[49-53] However, the relative importance of these cytokines in DHF is still unknown. Studies have shown that the pattern of cytokine response may be related to the pattern of cross-recognition of dengue-specific T-cells. Cross-reactive T-cells appear to be functionally deficit in their cytolytic activity but express enhanced cytokine production including TNF-a, IFN-g and chemokines.[54,55,56] Of note, TNF-a has been implicated in some severe manifestations including haemorrhage in some animal models.[57,58] Increase in vascular permeability can also be mediated by the activation of the complement system. Elevated levels of complement fragments have been documented in DHF.[59] Some complement fragments such as C3a and C5a are known to have permeability enhancing effects. In recent studies, the NS1 antigen of dengue virus has been shown to regulate complement activation and may play a role in the pathogenesis of DHF.[46,47,48]

Higher levels of viral load in DHF patients in comparison with DF patients have been demonstrated in many studies.[60,61] The levels of viral protein, NS1, were also higher in DHF patients.[62] The degrees of viral load correlate with measurements of disease severity such as the amount of

pleural effusions and thrombocytopenia, suggesting that viral burden may be a key determinant of disease severity.

4.4 Clinical laboratory findings of DHF

- The white blood cell (WBC) count may be normal or with predominant neutrophils in the early febrile phase. Thereafter, there is a drop in the total number of white blood cells and neutrophils, reaching a nadir towards the end of the febrile phase. The change in total white cell count (≤5000 cells/mm^3)[63] and ratio of neutrophils to lymphocyte (neutrophils<lymphocytes) is useful to predict the critical period of plasma leakage. This finding precedes thrombocytopenia or rising haematocrit. A relative lymphocytosis with increased atypical lymphocytes is commonly observed by the end of the febrile phase and into convalescence. These changes are also seen in DF.
- The platelet counts are normal during the early febrile phase. A mild decrease could be observed thereafter. A sudden drop in platelet count to below 100 000 occurs by the end of the febrile phase before the onset of shock or subsidence of fever. The level of platelet count is correlated with severity of DHF. In addition there is impairment of platelet function. These changes are of short duration and return to normal during convalescence.
- The haematocrit is normal in the early febrile phase. A slight increase may be due to high fever, anorexia and vomiting. A sudden rise in haematocrit is observed simultaneously or shortly after the drop in platelet count. Haemoconcentration or rising haematocrit by 20% from the baseline, e.g. from haematocrit of 35% to ≥42% is objective evidence of leakage of plasma.
- Thrombocytopenia and haemoconcentration are constant findings in DHF. A drop in platelet count to below 100 000 cells/mm^3 is usually found between the 3rd and 10th days of illness. A rise in haematocrit occurs in all DHF cases, particularly in shock cases. Haemoconcentration with haematocrit increases by 20% or more is objective evidence of plasma leakage. It should be noted that the level of haematocrit may be affected by early volume replacement and by bleeding.
- Other common findings are hypoproteinemia/albuminaemia (as a consequence of plasma leakage), hyponatremia, and mildly elevated serum aspartate aminotransferase levels (≤200 U/L) with the ratio of AST:ALT>2.
- 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 antiplasmin (plasmin inhibitor) has been noted in some cases. In severe cases with marked liver dysfunction, reduction is observed in the vitamin K-dependent prothrombin co-factors, such as factors V, VII, IX and X.
- Partial thromboplastin time and prothrombin time are prolonged in about half and one third of DHF cases respectively. Thrombin time is also prolonged in severe cases.
- Hyponatremia is frequently observed in DHF and is more severe in shock.
- Hypocalcemia (corrected for hypoalbuminemia) has been observed in all cases of DHF, the level is lower in Grade 3 and 4.
- Metabolic acidosis is frequently found in cases with prolonged shock. Blood urea nitrogen is elevated in prolonged shock.

4.5 Criteria for clinical diagnosis of DHF/DSS

Clinical manifestations

- Fever: acute onset, high and continuous, lasting two to seven days in most cases.
- Any of the following haemorrhagic manifestations including a positive tourniquet test[g] (the most common), petechiae, purpura (at venepuncture sites), ecchymosis, epistaxis, gum bleeding, and haematemesis and/or melena.
- Enlargement of the liver (hepatomegaly) is observed at some stage of the illness in 90%–98% of children. The frequency varies with time and/or the observer.
- Shock, manifested by tachycardia, poor tissue perfusion with weak pulse and narrowed pulse pressure (20 mmHg or less) or hypotension with the presence of cold, clammy skin and/or restlessness.

Laboratory findings

- Thrombocytopenia (100 000 cells per mm^3 or less)[h].
- Haemoconcentration; haematocrit increase of ≥20%[i] from the baseline of patient or population of the same age.

The first two clinical criteria, plus thrombocytopenia and haemoconcentration or a rising haematocrit, are sufficient to establish a clinical diagnosis of DHF. The presence of liver enlargement in addition to the first two clinical criteria is suggestive of DHF before the onset of plasma leakage.

The presence of pleural effusion (chest X-ray or ultrasound) is the most objective evidence of plasma leakage while hypoalbuminaemia provides supporting evidence. This is particularly useful for diagnosis of DHF in the following patients:

- anaemia.
- severe haemorrhage.
- where there is no baseline haematocrit.
- rise in haematocrit to <20% because of early intravenous therapy.

In cases with shock, a high haematocrit and marked thrombocytopenia support the diagnosis of DSS. A low ESR (<10 mm/first hour) during shock differentiates DSS from septic shock.

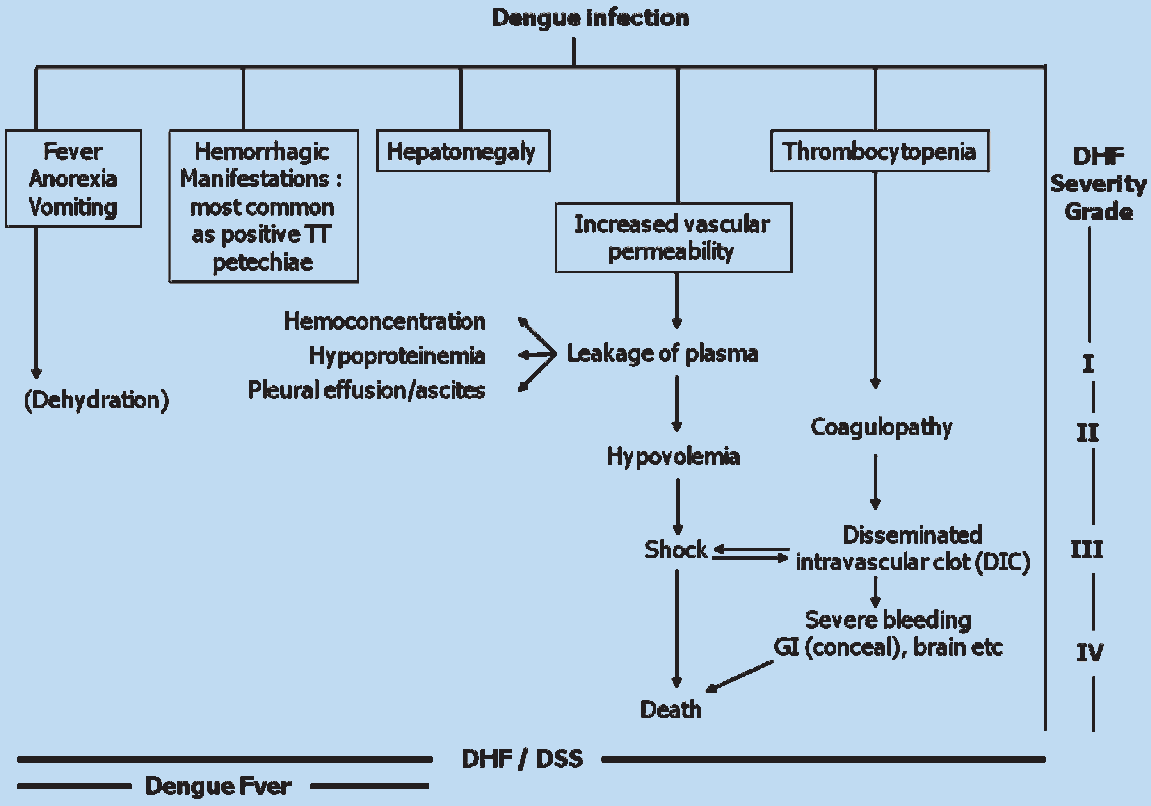
The clinical and laboratory findings associated with the various grades of severity of DHF are shown in *Box 7*.

g The tourniquet test is performed by inflating a blood pressure cuff to a point midway between the systolic and diastolic pressures for five minutes. The test is considered positive when 10 or more petechiae per sq. inch are observed. In DHF the test usually gives a definite positive result with 20 petechiae or more. The test may be negative or only mildly positive in obese patients and during the phase of profound shock. It usually becomes positive, sometimes strongly positive after recovery from shock.

h This level is usually observed shortly before subsidence of fever and/or onset of shock. Therefore, serial platelet estimation is essential for diagnosis. A few cases may have platelet count above 100 000 mm^3 at this period.

i Direct count using a phase-contrast microscope (normal 200 000-500 000/mm^3). In practice, for outpatients, an approximate count from a peripheral blood smear is acceptable. In normal persons, 5–10 platelets per oil-immersion field (the average observed from 10 fields is recommended) indicate an adequate platelet count. An average of 2–3 platelets per oil-immersion field or less is considered low (less than 100 000/mm^3).

Box 7: Major manifestations/pathophysiological change of DHF[j]



4.6 Grading the severity of DHF

The severity of DHF is classified into four grades[36,41] *(Table 4)*. The presence of thrombocytopenia with concurrent haemoconcentration differentiates Grade I and Grade 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 South-East Asia, Western Pacific and America Regions of WHO. Experiences in Cuba, Puerto Rico and Venezuela suggest that this classification is also useful for adults.

4.7 Differential diagnosis of DHF

Early in the febrile phase, the differential diagnoses include a wide spectrum of viral, bacterial and protozoal infections similar to that of DF. Haemorrhagic manifestations, e.g. positive tourniquet test and leucopenia ($\leq$5000 cells/mm^3)[63] suggest dengue illness. The presence of thrombocytopenia with concurrent haemoconcentration differentiates DHF/DSS from other diseases. In patients with no significant rise in haematocrit as a result of severe bleeding and/or early intravenous fluid therapy, demonstration of pleural effusion/ascites indicates plasma leakage. Hypoproteinaemia/albuminaemia supports the presence of plasma leakage. A normal erythrocyte sedimentation rate (ESR) helps differentiate dengue from bacterial infection and septic shock. It should be noted that during the period of shock, the ESR is <10 mm/hour.[64]

j Refer to section 4.6 for description of DHF severity grades.

Table 4: WHO classification of dengue infections and grading of severity of DHF

DF/ DHF	Grade	Signs and Symptoms	Laboratory
DF		Fever with two of the following: • Headache. • Retro-orbital pain. • Myalgia. • Arthtralgia/bone pain. • Rash. • Haemorrhagic manifestations. • **No evidence of plasma leakage**.	• Leucopenia (wbc ≤5000 cells/mm^3). • Thrombocytopenia (Platelet count <150 000 cells/mm^3). • Rising haematocrit (5% – 10%). • No evidence of plasma loss.
DHF	I	Fever and haemorrhagic manifestation (positive tourniquet test) and **evidence of plasma leakage**	Thrombocytopenia <100 000 cells/ mm^3; HCT rise ≥20%
DHF	II	As in Grade **I plus** spontaneous bleeding.	Thrombocytopenia <100 000 cells/mm^3; HCT rise ≥20%.
DHF#	III	As in Grade **I or II plus** circulatory failure (weak pulse, narrow pulse pressure (≤20 mmHg), hypotension, restlessness).	Thrombocytopenia <100 000 cells/mm^3; HCT rise ≥20%.
DHF#	IV	As in Grade **III** plus profound shock with undetectable BP and pulse	Thrombocytopenia < 100 000 cells/mm^3; HCT rise ≥20%.

Source: http://www.who.int/csr/resources/publications/dengue/Denguepublication/en/

#: DHF III and IV are DSS

4.8 Complications

DF complications

DF with haemorrhage can occur in association with underlying disease such as peptic ulcers, severe thrombocytopenia and trauma.

DHF is not a continuum of DF.

DHF complications

These occur usually in association with profound/prolonged shock leading to metabolic acidosis and severe bleeding as a result of DIC and multiorgan failure such as hepatic and renal dysfunction. More important, excessive fluid replacement during the plasma leakage period leads to massive effusions causing respiratory compromise, acute pulmonary congestion and/or heart failure. Continued fluid therapy after the period of plasma leakage will cause acute pulmonary oedema or heart failure, especially when there is reabsorption of extravasated fluid. In addition, profound/prolonged shock and inappropriate fluid therapy can cause metabolic/electrolyte disturbance. Metabolic abnormalities are frequently found as hypoglycemia, hyponatremia, hypocalcemia and occasionally, hyperglycemia. These disturbances may lead to various unusual manifestations, e.g. encephalopathy.

4.9 Expanded dengue syndrome (unusual or atypical manifestations)

Unusual manifestations are uncommon. In recent years with the geographical spread of dengue illness and with more involvement of adults, there have been increasing reports of DF and DHF with unusual manifestations. These include: neurological, hepatic, renal and other isolated organ involvement. These could be explained as complications of severe profound shock or associated with underlying host conditions/diseases or coinfections.

Central nervous system (CNS) manifestations including convulsions, spasticity, changes in consciousness and transient paresis have been observed. The underlying causes depend on the timing of these manifestations in relation to the viremia, plasma leakage or convalescence.

Encephalopathy in fatal cases has been reported in Indonesia, Malaysia, Myanmar, India and Puerto Rico. However, in most cases there have been no autopsies to rule out bleeding or occlusion of the blood vessels. Although limited, there is some evidence that on rare occasions dengue viruses may cross the blood-brain barrier and cause encephalitis. It should be noted that exclusion of concurrent infections has not been exhaustive. *Table 5* details the unusual/atypical manifestations of dengue.

The above-mentioned unusual manifestations may be underreported or unrecognized or not related to dengue. However, it is essential that proper clinical assessment is carried out for appropriate management, and causal studies should be done.

4.10 High-risk patients

The following host factors contribute to more severe disease and its complications:

- infants and the elderly,
- obesity,
- pregnant women,
- peptic ulcer disease,
- women who have menstruation or abnormal vaginal bleeding,
- haemolytic diseases such as glucose-6-phosphatase dehydrogenase (G-6PD) deficiency, thalassemia and other haemoglobinopathies,
- congenital heart disease,
- chronic diseases such as diabetes mellitus, hypertension, asthma, ischaemic heart disease, chronic renal failure, liver cirrhosis,
- patients on steroid or NSAID treatment, and
- others.

Table 5: Expanded dengue syndrome (Unusual or atypical manifestations of dengue)

System	Unusual or atypical manifestations
Neurological	Febrile seizures in young children. Encephalopathy. Encephalitis/aseptic meningitis. Intracranial haemorrhages/thrombosis. Subdural effusions. Mononeuropathies/polyneuropathies/Guillane-Barre Syndrome. Transverse myelitis.
Gastrointestinal/hepatic	Hepatitis/fulminant hepatic failure. Acalculous cholecystitis. Acute pancreatitis. Hyperplasia of Peyer's patches. Acute parotitis.
Renal	Acute renal failure. Hemolytic uremic syndrome.
Cardiac	Conduction abnormalities. Myocarditis. Pericarditis.
Respiratory	Acute respiratory distress syndrome. Pulmonary haemorrhage.
Musculoskeletal	Myositis with raised creatine phosphokinase (CPK). Rhabdomyolysis.
Lymphoreticular/bone marrow	Infection associated haemophagocytic syndrome. IAHS or Haemophagocytic lymphohistiocytosis (HLH), idiopathic thrombocytopenic purura (ITP). Spontaneous splenic rupture. Lymph node infarction.
Eye	Macular haemorrhage. Impaired visual acuity. Optic neuritis.
Others	Post-infectious fatigue syndrome, depression, hallucinations, psychosis, alopecia.

Source: Gulati S., Maheshwari A. Atypical manifestations of dengue. *Trop Med Int Health.* 2007 Sep.; 12(9):1087 – 95.[65]

4.11 Clinical manifestations of DF/DHF in adults

Compared with children, adults with DF have more severe manifestations such as incapacitating headache and muscle, joint and bone pain. Depression, insomnia and post-infectious fatigue may cause prolonged recovery. Sinus bradycardia and arrhythmias during convalescence are more common in adults than in children.

Generally, the percentage of DHF in adults is lower than in children. Adults with DHF have a course similar to that in children. However, some studies have mentioned less severe plasma leakage in adult patients. Yet there are some countries where most deaths are seen in adults, which could be explained by the late recognition of DHF/shock and the higher incidence of bleeding with delayed blood transfusion. Adult patients with shock have been reported to be able to work until the stage of profound shock.

In addition, patients self-medicate with analgesics such as paracetamol, NSAIDs, anti-emetic and other drugs that worsen liver and platelet functions. Sometimes fever may not be detected by adult patients themselves. They are more likely to have the risk factors for severe disease such as peptic ulcer disease and others as stated above. A summary of diagnosis of DF and DHF is presented in *Box 8a-8c*.[39]

Box 8a: Diagnosis of dengue fever and dengue haemorrhagic fever[k]

Dengue fever

Probable diagnosis:

Acute febrile illness with two or more of the following[l]:

- headache,
- retro-orbital pain,
- myalgia,
- arthralgia/bone pain,
- rash,
- haemorrhagic manifestations,
- leucopenia (wbc $\leq$5000 cells/mm^3),
- thrombocytopenia (platelet count <150 000 cells/mm^3),
- rising haematocrit (5 – 10%);

and at least one of following:

- supportive serology on single serum sample: titre $\geq$1280 with haemagglutination inhibition test, comparable IgG titre with enzyme-linked immunosorbent assay, or tasting positive in IgM antibody test, and
- occurrence at the same location and time as confirmed cases of dengue fever.

Confirmed diagnosis:

Probable case with at least one of the following:

- isolation of dengue virus from serum, CSF or autopsy samples.
- fourfold or greater increase in serum IgG (by haemagglutination inhibition test) or increase in IgM antibody specific to dengue virus.
- detection of dengue virus or antigen in tissue, serum or cerebrospinal fluid by immunohistochemistry, immunofluorescence or enzyme-linked immunosorbent assay.
- detection of dengue virus genomic sequences by reverse transcription-polymerase chain reaction.

k Based on discussions and recommendations of the Consultative Meeting on Dengue Case Classication and Case Management held in Bangkok, Thailand, on 7-8 October 2010. .The participants included experts from SEARO and WPRO countries and one observer each from University of Massachusetts Medical School, USA and Armed Forces Research Institute of Medical Sciences, Thailand, and secretariat from the WHO Collaborating Centre for Case Management of Dengue/DHF/DSS, QSNICH (Bangkok, Thailand).

l Studies have shown that in endemic areas acute febrile illness with a positive TT and leucopenia (WBC$\leq$5000 cells/mm^3) has a good positive predictive value of 70% to 80%. In situations where serology is not available, these are useful for early detection of dengue cases.[37,38]

Box 8b: Dengue haemorrhagic fever

All of following[m]:

- acute onset of fever of two to seven days duration.
- haemorrhagic manifestations, shown by any of the following: positive tourniquet test, petechiae, ecchymoses or purpura, or bleeding from mucosa, gastrointestinal tract, injection sites, or other locations.
- platelet count ≤100 000 cells/mm^3
- objective evidence of plasma leakage[n] due to increased vascular permeability shown by any of the following:
  - Rising haematocrit/haemoconcentration ≥20% from baseline or decrease in convalescence, or evidence of plasma leakage such as pleural effusion, ascites or hypoproteinaemia/albuminaemia.[39]

Box 8c: Dengue shock syndrome

Criteria for dengue haemorrhagic fever as above with signs of shock including:

- tachycardia, cool extremities, delayed capillary refill, weak pulse, lethargy or restlessness, which may be a sign of reduced brain perfusion.
- pulse pressure ≤20 mmHg with increased diastolic pressure, e.g. 100/80 mmHg.
- hypotension by age, defined as systolic pressure <80 mmHg for those aged <5 years or 80 to 90 mmHg for older children and adults.

m If all the four criteria are met, the sensitivity and specificity is 62% and 92% respectively. Anon S. et al. Dengue Hemorrhagic Fever: The Sensitivity and Specificity of the World Health Organization Definition for Identification of Severe Cases of Dengue in Thailand, 1994–2005, Clin. Inf. Dis. 2010; 50 (8):1135-43.

n If fever and significant plasma leakage are documented, a clinical diagnosis of DHF is most likely even if there is no bleeding or thrombocytopenia.

5. Laboratory Diagnosis

Rapid and accurate dengue diagnosis is of paramount importance for: (i) epidemiological surveillance; (ii) clinical management; (iii) research; and (iv) vaccine trials. Epidemiological surveillance requires early determination of dengue virus infection during the outbreak for urgent public health action towards control as well as at sentinel sites for detection of circulating serotypes/genotypes during the inter-epidemic periods for use in forecasting possible outbreaks. Clinical management requires early diagnosis of cases, confirmation of clinical diagnosis and for differential diagnosis from other flaviviruses/infection agents.

The following laboratory tests are available to diagnose dengue fever and DHF:

- Virus isolation
  - serotypic/genotypic characterization
- Viral nucleic acid detection
- Viral antigen detection
- Immunological response based tests
  - IgM and IgG antibody assays
- Analysis for haematological parameters

5.1 Diagnostic tests and phases of disease

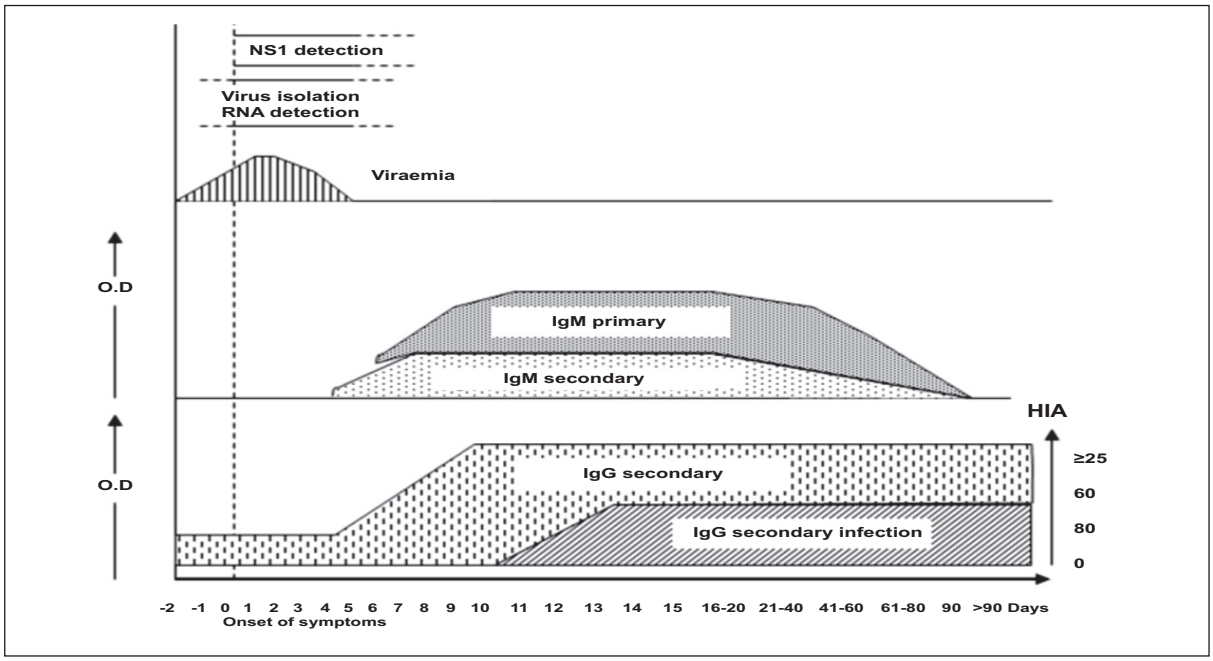
Dengue viraemia in a patient is short, typically occurs 2–3 days prior to the onset of fever and lasts for four to seven days of illness. During this period the dengue virus, its nucleic acid and circulating viral antigen can be detected (*Figure 5*).

Antibody response to infection comprises the appearance of different types of immunoglobulins; and IgM and IgG immunoglobulin isotypes are of diagnostic value in dengue. IgM antibodies are detectable by days 3–5 after the onset of illness, rise quickly by about two weeks and decline to undetectable levels after 2–3 months. IgG antibodies are detectable at low level by the end of the first week, increase subsequently and remain for a longer period (for many years). Because of the late appearance of IgM antibody, i.e. after five days of onset of fever, serological tests based on this antibody done during the first five days of clinical illness are usually negative.

During the secondary dengue infection (when the host has previously been infected by dengue virus), antibody titres rise rapidly. IgG antibodies are detectable at high levels, even in the initial phase, and persist from several months to a lifelong period. IgM antibody levels are significantly lower in secondary infection cases. Hence, a ratio of IgM/IgG is commonly used to differentiate between primary and secondary dengue infections. Thrombocytopenia is usually observed between the third and eighth day of illness followed by other haematocrit changes.

Figure 5 shows the timeline of primary and secondary dengue virus infections and the diagnostic methods that can be used to detect infection at a particular time of illness.

Figure 5: Approximate timeline of primary and secondary dengue virus infections and the diagnostic methods that can be used to detect infection



Source: *WHO. Dengue Guidelines for Diagnosis, Treatment, Prevention and Control, New edition, 2009. WHO Geneva.*[66]

5.2 Specimens: Collection, storage and shipment

An essential aspect of laboratory diagnosis of dengue is proper collection, processing, storage and shipment of clinical specimens. The type of specimens and their storage and shipment requirements are shown in *Table 6*.

Table 6: Collection, storage and shipment requirements of specimens

Specimen type	Time of collection	Clot retraction	Storage	Shipment
Acute phase blood (S1)	0–5 days after onset	2–6 hours, 4 °C	Serum –70 °C	Dry ice
Recovery (convalescent) phase blood (S2+S3)	14–21 days after onset	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

Source: Gubler D.J., Sather G.E.. Laboratory diagnosis of dengue and dengue haemorrhagic fever. Proceedings of the International Symposium on Yellow Fever and Dengue; 1988; Rio de Janeiro, Brazil.[67]

Serological diagnosis using certain methods is arrived at based on the identification of changes in specific antibody levels in paired specimens. Hence serial (paired) specimens are required to confirm or refute a diagnosis of acute flavivirus or dengue infection.

Collection of specimens is done at different time intervals as mentioned below:

- Collect a specimen as soon as possible after the onset of illness, hospital admission or attendance at a clinic (this is called the acute phase specimen, S1).
- Collect a specimen shortly before discharge from the hospital or, in the event of a fatality, at the time of death (convalescent phase specimen, S2).
- Collect a third specimen, in the event hospital discharge occurs within 1–2 days of the subsidence of fever, 7–21 days after the acute serum was drawn (late convalescent phase specimen, S3).

The optimal interval between paired sera, i.e. the acute (S1) and the convalescent (S2 or S3) blood specimen, is 10–14 days.

- Samples of request and reporting forms for dengue laboratory examination are provided in Annex 1. Blood is preferably collected in tubes or vials, but filter paper may be used if this is the only option. Filter paper samples are not suitable for virus isolation.

Blood collection in tubes or vials

The following are the steps for blood collection in tubes or vials:

- Collect 2 ml–10 ml of venous blood with aseptic precautions.
- Use adhesive tape marked with pencil, indelible ink, or a typewritten/printed self-adhesive label to identify the container. The name of the patient, identification number and date of collection must be indicated on the label.
- Use vacuum tubes or sterile vials with screw caps and gasket, if possible, for collection. Secure the cap with adhesive tape, wax or other sealing material to prevent leakage during transport.
- In case of an anticipated delay of more than 24 hours before specimens can be submitted to the laboratory, separate the serum from the red blood cells and store frozen. Do not freeze whole blood as haemolysis may interfere with serology test results.
- Ship specimens to the laboratory on wet ice (blood) or dry ice (serum) as soon as possible.
- The shipment should adhere to national/international guidelines on shipment of infectious material.

Blood collection on filter paper

The following are the steps for blood collection on filter paper:

- With a pencil, write the patient's initials or number on two or three filter-paper discs or strips of standardized absorbent paper[o].
- Collect sufficient fingertip blood (or venous blood using a syringe) on the filter paper to fully saturate it through to the reverse side. Most standard filter paper discs or strips will absorb 0.1 ml of serum.
- Allow the discs or strips to dry in a place that is protected from direct sunlight and insects. Preferably, the blood-soaked papers should be placed in a stand which allows aeration of both sides. For unusually thick papers, a drying chamber may be useful, e.g. desiccator jar, air-conditioned room or warm-air incubator.

o Whatman No. 3 filter paper discs 12.7 mm (½ inch) in diameter are suitable for this purpose, or Nobuto type-1 blood-sampling paper made by Toyo Roshi Kaisha Ltd, Tokyo, Japan.

- Place the dried strips in plastic bags along with a silica bead sachet if possible, and staple them to the "Laboratory Examination Request" form. Store without refrigeration. Dried filter paper discs may be sent through postal mail.

Serum elution in the laboratory: *One of the recommended methods for eluting the blood from filter paper discs is mentioned below:*

- Elute the disc at room temperature for 60 minutes, or at 4 °C overnight, in 1 ml of kaolin in borate saline (125 g/litre), pH 9.0, in a test-tube.
- After elution, keep the tube at room temperature for 20 minutes, shaking it periodically.
- Centrifuge for 30 minutes at 600 g.
- For haemagglutination inhibition (HI) test using goose erythrocytes, without removing the kaolin add 0.05 ml of 50% suspension of goose cells to the tube, shake without disturbing the pellet, and incubate at 37 °C for 30 minutes.
- For IgG and IgM assays, elute discs/strips in phosphate buffered saline (PBS) containing 0.5% Tween 20 and 5% non-fat dried milk for two hours at room temperature.
- Centrifuge at 600 g for 10 minutes and decant the supernatant.
- The supernatant is equivalent to a 1:30 serum dilution.

Each laboratory must standardize the filter paper technique prior to using it in diagnostic services, using a panel of well characterized sera samples.

5.3 Diagnostic methods for detection of dengue infection

During the early stages of the disease (up to six days of onset of illness), virus isolation, viral nucleic acid or antigen detection can be used to diagnose infection. At the end of the acute phase of infection, immunological tests are the methods of choice for diagnosis.

Isolation of virus

Isolation of dengue virus from clinical specimens is possible provided the sample is taken during the first six days of illness and processed without delay. Specimens that are suitable for virus isolation include: acute phase serum, plasma or washed buffy coat from the patient, autopsy tissues from fatal cases (especially liver, spleen, lymph nodes and thymus), and mosquitoes collected from the affected areas.

For short periods of storage (up to 48 hours), specimens to be used for virus isolation can be kept at +4 °C to +8 °C. For longer storage the serum should be separated and frozen at –70 °C and maintained at such a temperature that thawing does not occur. If isolation from leucocytes is to be attempted, heparinized blood samples should be delivered to the laboratory within a few hours. Whenever possible, original material (viraemic serum or infected mosquito pools) as well as laboratory-passaged materials should be preserved for future study.

Tissues and pooled mosquitoes are triturated or sonicated prior to inoculation. Different methods of inoculation and methods of confirming the presence of dengue virus are shown in Table 7.[50] The choice of methods for isolation and identification of dengue virus will depend on local availability of mosquitoes, cell culture and laboratory capability. Inoculation of serum or plasma into mosquitoes is the most sensitive method of virus isolation, but mosquito cell culture is the most cost-effective method for routine virological surveillance. It is essential for health workers interested in making a diagnosis by means of virus isolation to contact the appropriate virology laboratory prior to the collection of specimens. The acquisition, storage and shipment of the samples can then be organized to have the best chances of successful isolation.

Table 7: Dengue virus isolation methods

Recommended methods	Confirmation of dengue virus infection
• Inoculation of mosquitoes (*Aedes aegypti, Ae. albopictus, Toxorhynchites amboinensis* and *Toxorhynchites splendens*).	• Dengue virus generally replicates to high titres (10^6 to 10^7 MID in an hour to five days).[p] • Presence of antigens in head squashes demonstrated by immunofluorescence (IFA) [Riman's test is the gold standard].
• Inoculation of insect cell cultures, namely C6/36, a clone of *Ae. albopictus* cells. • Inoculation of mammalian cultures, namely vero cells, LLCMK2 and BHK21.	• Presence of antigens in cells demonstrated by immunofluorescence (IFA). Viral titre is done by RT-PCR. • Cytopathic effect and plaque formation in mammalian cells – less efficient.

Source: Vorndam V., Kuno G.. Laboratory diagnosis of dengue virus infection. In: Gubler D.J., Kuno G., Editors. Dengue and dengue haemorrhagic fever. Wallingford, Oxon: CAB International; 1997. p. 313-34.[68]

In order to identify different dengue virus serotypes, mosquito head squashes and slides of infected cell cultures are examined by indirect immunoflourescence using serotype-specific monoclonal antibodies.

Currently, cell culture is the most widely used method for dengue virus isolation. The mosquito cell line C6/36 or AP61 are the host cells of choice for isolation of dengue viruses. Inoculation of suckling mice or mosquitoes can be attempted when no other method is available.

The isolation and confirmation of the identity of the virus requires substantial skills, competency and an infrastructure with BSL2/BSL3 facilities.

Viral nucleic acid detection

Dengue viral genome, which consists of ribonucleic acid (RNA), can be detected by reverse transcripatse polymerase chain reaction (RT-PCR) assay. RNA is heat-labile and, therefore, specimens for nucleic acid detection must be handled and stored according to procedures described for virus isolation.

Reverse transcriptase-polymerase chain reaction (RT-PCR)

In recent years, a number of RT-PCR assays have been reported for detecting dengue virus. They offer better specificity and sensitivity compared with virus isolation with a much more rapid turnaround time. A BSL2 laboratory with equipment for molecular biology and skilled professionals are needed to carry out this test.

All nucleic acid detection assays involve three basic steps: (i) nucleic acid extraction and purification; (ii) amplification of the nucleic acid; and (iii) detection of the amplified product. False positive results can occur, and this can be prevented by proper isolation of different steps of the assay and observing strict decontamination procedures.

p Disadvantages include hard work, need for insectaries to produce a large number of mosquitoes and the isolation precautions to avoid release of infected mosquitoes. However, *Toxorhynchitis* larvae can be used for inoculation to avoid accidental release of infected mosquitoes.

Nested RT-PCR

Nested RT-PCR assay involves using universal dengue primers targeting the C/prM region of the viral genome for an initial reverse transcription and amplification step, followed by a nested PCR amplification that is serotype-specific.

One-step multiplex RT-PCR

This test is an alternative to nested RT-PCR. A combination of the four serotype-specific oligonucleotide primers is used in a single reaction step in order to identify the serotype. The products of these reactions are separated by electrophoresis on an agarose gel, and the amplification products are visualized as bands of different molecular weights after staining the gel using ethidium bromide dye, and compared with standard molecular weight markers. In this assay, dengue serotypes are identified by the size of their bands.

Real-time RT-PCR

The real-time RT-PCR assay is also a one-step assay system using primer pairs and probes that are specific to each dengue serotype. The use of a fluorescent probe enables the detection of the reaction products in real time, in a specialized PCR machine, without the need for electrophoresis. Real-time RT-PCR assays are either "singleplex" (detecting only one serotype at a time) or "multiplex" (able to identify all four serotypes from a single sample). These tests offer high-throughput and hence are very useful for large-scale surveillance.

Isothermal amplification method

The NASBA (nucleic acid sequence-based amplification) assay is an isothermal RNA-specific amplification assay that does not require thermal cycling instrumentation. The initial stage is a reverse transcription in which the single-stranded RNA target is copied into a double-stranded DNA molecule that serves as template for RNA transcription. Amplified RNA is detected either by electrochemiluminescence or in real time with fluorescent-labelled molecular beacon probes.

Compared with virus isolation, the sensitivity of the RT-PCR methods varies from 80% to 100% and depends upon the region of the genome targeted by the primers, the approach used to amplify or detect PCR products and the methods employed for subtyping. The advantages of this technology include high sensitivity and specificity, ease of identifying serotypes and early detection of the infection. It is, however, an expensive technology that requires sophisticated instrumentation and skilled manpower.

Recently, Loop Mediated Amplification (LAMP) PCR method has been developed, which promises an easy-to-do and less expensive instrumentation alternative for RT-PCR and real-time PCR assays. However, its performance needs to be compared with that of latter nucleic acid methods.[69]

Viral antigen detection

The NS1 gene product is a glycoprotein produced by all flaviviruses and is essential for replication and viability of the virus. The protein is secreted by mammalian cells but not by insect cells. NS1 antigen appears as early as Day 1 after the onset of the fever and declines to undetectable levels by 5–6 days. Hence, tests based on this antigen can be used for early diagnosis.

ELISA and dot blot assays directed against the envelop/membrane (EM) antigens and nonstructural protein 1 (NS1) demonstrated that this antigen is present in high concentrations in the sera of the dengue virus-infected patients during the early clinical phase of the disease (*Figure 5*) and can be detected in both patients with primary and secondary dengue infections for up to six days after the onset of

the illness. Commercial kits for the detection of NS1 antigens are now available; however, these kits do not differentiate between the serotypes. Besides providing an early diagnostic marker for clinical management, it may also facilitate the improvement of epidemiological surveys of dengue infection.

5.4 Immunological response and serological tests

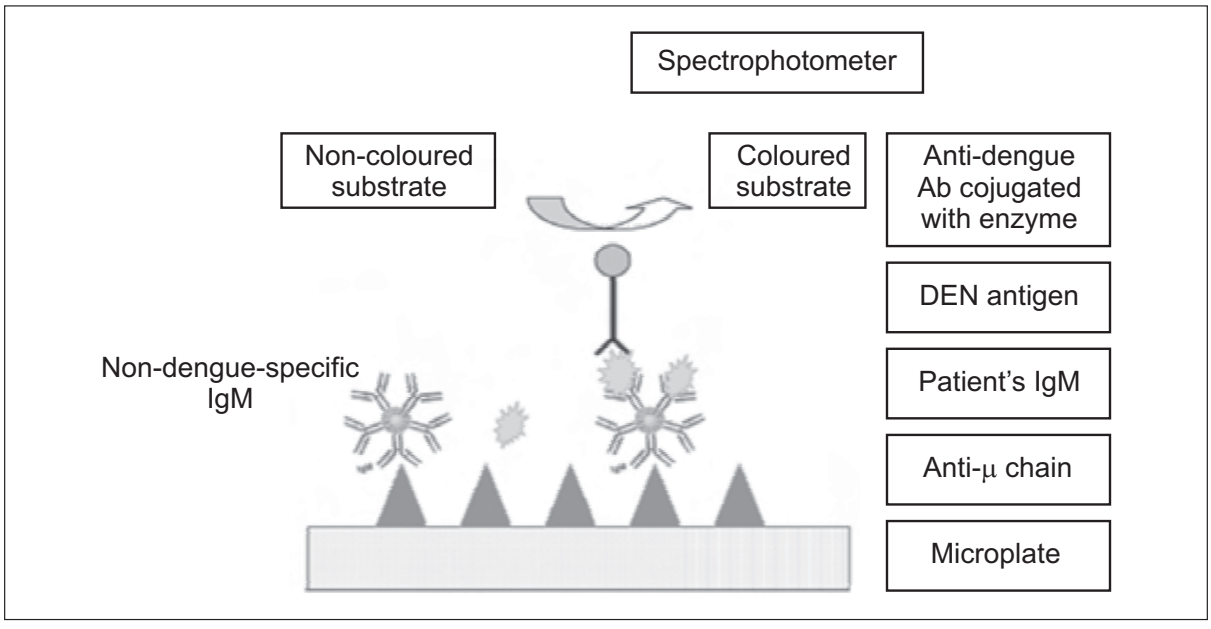
Five basic serological tests are used for the diagnosis of dengue infection.[67,70] These are: haemagglutination-inhibition (HI), complement fixation (CF), neutralization test (NT), IgM capture enzyme-linked immunosorbent assay (MAC-ELISA), and indirect IgG ELISA. For tests other than those that detect IgM, unequivocal serological confirmation depends upon a significant (four-fold or greater) rise in specific antibodies between acute-phase and convalescent-phase serum samples. The antigen battery for most of these serological tests should include all four dengue serotypes, another flavivirus, such as Japanese encephalitis, a non-flavivirus such as chikungunya, and an uninfected tissue as control antigen, when possible.

IgM-capture enzyme-linked immunosorbent assay (MAC-ELISA)

MAC-ELISA has become widely used in the past few years. It is a simple and rapid test that requires very little sophisticated equipment. MAC-ELISA is based on detecting the dengue-specific IgM antibodies in the test serum by capturing them out of solution using anti-human IgM that was previously bound to the solid phase.[42] If the patient's serum has antidengue 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-labelled anti-dengue antibody, which may be human or monoclonal antibody. An enzyme-substrate is added to produce a colour reaction.

The anti-dengue IgM antibody develops a little earlier than IgG, and is usually detectable by Day 5 of the illness, i.e. the antibody is not usually detectable during the first five days of illness. However, the time of appearance of IgM antibody varies considerably among patients. IgM antibody titers in primary infections are significantly higher than in secondary infections, although it is not uncommon to obtain IgM titers of 320 in the latter cases. In some primary infections, detectable IgM may persist for more than 90 days, but in most patients it wanes to an undetectable level by 60 days (*Figure 6*).

Figure 6: Principle of MAC-ELISA test



Source: Dengue Guidelines for Diagnosis, Treatment, Prevention and Control, New edition, 2009, WHO Geneva.[66]

MAC-ELISA is slightly less sensitive than the HI test for diagnosing dengue infection. It has the advantage, however, of frequently requiring only a single, properly timed blood sample. Considering the difficulty in obtaining second blood samples and the long delay in obtaining conclusive results from the HI test, this low error rate would be acceptable in most surveillance systems. It must be emphasized, however, that because of the persistence of IgM antibody, MAC-ELISA positive results 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 had a dengue infection sometime in the previous two to three months.

MAC-ELISA has become an invaluable tool for surveillance of DF, DHF and DSS. In areas where dengue is not endemic, it can be used in clinical surveillance for viral illness or for random, population-based serosurveys, with the certainty that any positives detected are recent infections.[67] It is especially useful for hospitalized patients who are generally admitted at a late stage of illness after detectable IgM is already present in the blood.

IgG-ELISA

An indirect IgG-ELISA has been developed and compares well with the HI test.[70] This test can also be used to differentiate primary and secondary dengue infections. The test is simple and easy to perform, and is thus useful for high-volume testing. The IgG-ELISA is very non-specific and exhibits the same broad cross-reactivity among flaviviruses as the HI test; it cannot be used to identify the infecting dengue serotype. These tests can be used independently or in combination, depending upon the type of the sample and test available in order to confirm the diagnosis as shown in *Table 8*.

Table 8: Interpretation of dengue diagnostic test

Highly suggestive	Confirmed
One of the following: (1) IgM+ve in a single serum sample. (2) IgG+ve in a single serum sample with a HI titre of 1280 or greater.	One of the following: (1) RT-PCR+ve. (2) Virus culture+ve. (3) IgM seroconversion in paired sera. (4) IgG seroconversion in paired sera or four-fold IgG titre increase in paired sera.

Source: Jaenisch T., Wills B. (2008) Results from the DENCO study. TDR/WHO Expert Meeting on Dengue Classification and Case Management. Implications of the DENCO study. WHO, Geneva, Sept. 30–Oct. 1 2008.[71]

IgM/IgG ratio

The IgM/IgG ratio is used to distinguish primary infection from secondary dengue infection . A dengue virus infection is defined as primary if the capture IgM/IgG ratio is greater than 1.2, or as secondary if the ratio is less than 1.2. This ratio testing system has been adopted by select commercial vendors. However, it has been recently demonstrated that the ratios vary depending on whether the patient has a serological non-classical or a classical dengue infection, and the ratios have been redefined taking into consideration the four subgroups of classical infection with dengue.[72] The adjusted ratios of greater than 2.6 and less than 2.6, established by these authors, correctly classified 100% of serologically classical dengue infections and 90% of serologically non-classical infections.

Haemagglutination inhibition test

Of the above tests, haemagglutination inhibition or HI test has been most frequently used in the past for routine serological diagnosis of dengue infections. It is sensitive and easy to perform, requires only minimal equipment, and is very reliable if properly done. Because HI antibodies persist for long periods (up to 50 years or longer), the test is ideal for sero-epidemiologic studies.

The major disadvantage of the HI test is lack of specificity, which makes it unreliable for identifying the infecting virus serotype. However, some primary infections may show a relatively monotypic HI response that generally corelates with the virus isolated.[67] In recent times not many laboratories are performing this test.

Complement fixation test

The *complement fixation or* CF test is not widely used for routine dengue diagnostic serology. It is more difficult to perform and requires highly trained personnel. The CF test is based on the principle that the complement is consumed during antigen-antibody reactions. Two reactions are involved, a test system and an indicator system. Antigens for the CF test are prepared in the same manner as those for the HI test. The CF test is useful for patients with current infections, but is of limited value for seroepidemiological studies where detection of persistent antibodies is important. Only a few laboratories conduct this assay.

Neutralization test

The *neutralization test or* NT is the most specific and sensitive serological test for dengue viruses used for determining the immune protection. The common protocol used in most dengue laboratories is the serum dilution plaque reduction neutralization test (PRNT). The major disadvantages of this technique are the expense and time required to perform the test, and the technical difficulty involved since it requires cell culture facility. It is, therefore, not routinely used in most laboratories. However, it is of great use in the development of vaccines and their efficacy trials.

5.5 Rapid diagnostic test (RDT)

A number of commercial rapid format serological test-kits for anti-dengue IgM and IgG antibodies have become available in the past few years, some of these producing results within 15 minutes.[70] Unfortunately, the accuracy of most of these tests is uncertain since they have not yet been properly validated. Rapid tests can yield false positive results due to cross-reaction with other flaviviruses, malaria parasite, leptospires and immune disorders such as rheumatoid and lupus. It is anticipated that these test kits can be reformulated to make them more specific, thus making global laboratory-based surveillance for DF/DHF an attainable goal in the near future. It is important to note that these kits should not be used in the clinical setting to guide the management of DF/DHF cases because many serum samples taken in the first five days after the onset of illness will not have detectable IgM antibodies. The tests would thus give a false negative result. Reliance on such tests to guide clinical management could, therefore, result in an increase in case-fatality rates.[q]

In an outbreak situation, if more than 50% of specimens test positive when rapid tests are used, dengue virus is then highly suggestive of being the cause of febrile outbreak.

q For further details, refer to: Update on the Principles and Use of Rapid Tests in Dengue, Prepared by the Malaria, Other Vector-borne and Parasitic Diseases Unit of the Western Pacific Region of WHO for dengue programme managers and health practitioners (2009).

5.6 Haematological tests

Standard haematological parameters such as platelet count and haematocrit are important and are part of the biological diagnosis of dengue infection. Therefore, they should be closely monitored.

Thrombocytopenia, a drop in platelet count below 100 000 per μl, may be occasionally observed in dengue fever but is a constant feature in DHF. Thrombocytopenia is usually found between the third and eighth day of illness often before or simultaneously with changes in haematocrit.

Haemoconcentration with an increase in the haematocrit of 20% or more (for the same patient or for a patient of the same age and sex) is considered to be a definitive evidence of increased vascular permeability and plasma leakage.

5.7 Biosafety practices and waste disposal

Handling of blood and tissues exposes health-care workers to the risk of contracting serious communicable diseases. Improper disposal of clinical and laboratory materials containing pathogens is a health risk to individuals as well as the community. To minimize these risks, health-care workers need to be trained and provided with appropriate infrastructure, especially personal protective material and equipment.[73]

5.8 Quality assurance

Laboratories undertaking dengue diagnosis work need to establish a functional quality system so that the results generated are reliable. Strengthening internal quality control and checking the quality of diagnostics using a panel of well-characterized samples at regular intervals will ensure accurate diagnosis.

Laboratories employing in-house diagnostics need to standardize the assay against well-characterized samples in order to ascertain sensitivity and specificity. Participating in an external quality assessment scheme can enhance the credibility of the laboratory and support the selection of appropriate public health action.

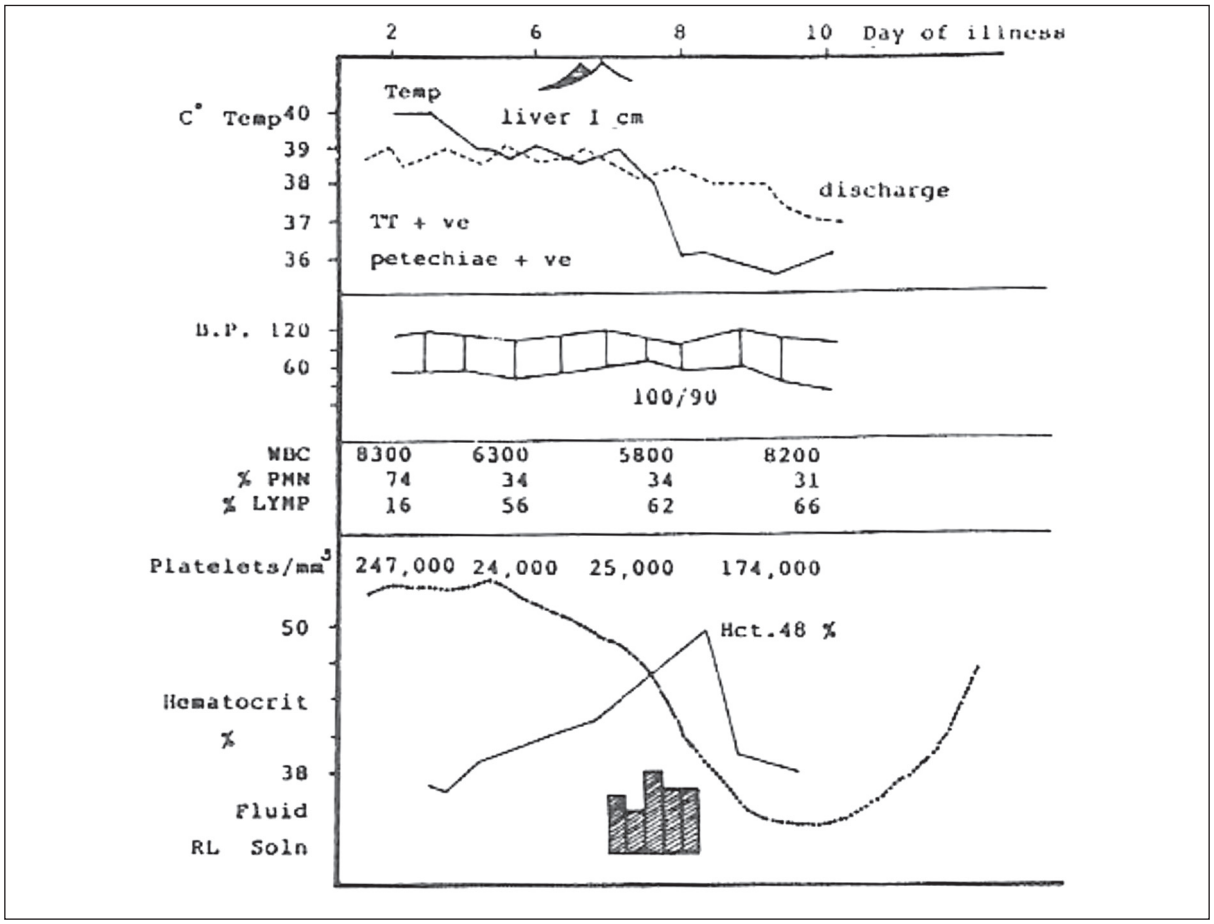
5.9 Network of laboratories

Every country should endeavour to establish a network of dengue diagnostic laboratories with a specific mandate for each level of the health laboratory. While the peripheral laboratories can undertake RDT and have the competence to collect, store and ship the material to the next higher level of laboratories, the national laboratories should perform genetic characterization of the virus, organize external quality assessment schemes, impart training and develop national guidelines. The national laboratories are also encouraged to join international networks such as the European Network for Diagnostics of "Imported" Viral Diseases (ENIVD) to draw support from the global community.

6. Clinical Management of Dengue/ Dengue Haemorrhagic Fever[r]

The clinical spectrum of dengue infection includes asymptomatic infection, DF and DHF, which is characterized by plasma leakage and haemorrhagic manifestations. At the end of the incubation period, the illness starts abruptly and is followed by three phases, the febrile, critical and recovery phase,[74] as depicted in the schematic representation below (*Figure 7*):

Figure 7: Course of dengue illness



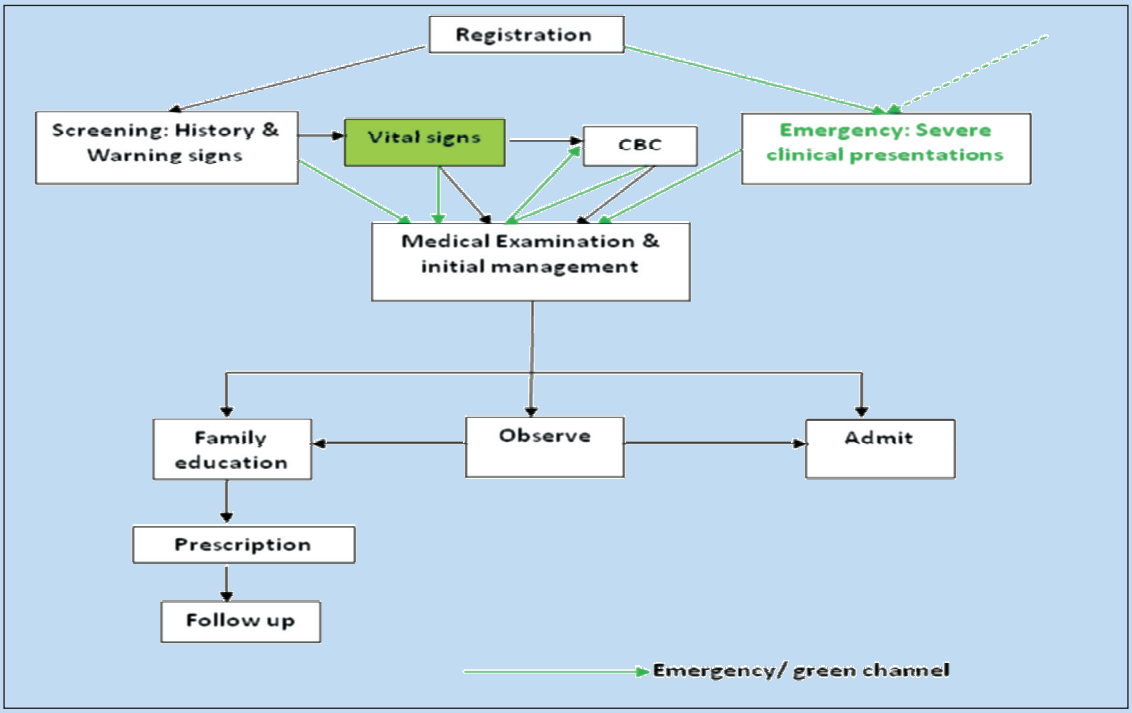
Source: Nimmannitya S.. Clinical manifestations and management of dengue/dengue haemorrhagic fever. In: Thongcharoen, P. Ed. Monograph on dengue/dengue haemorrhagic fever. WHO SEARO 1993, p 48–54, 55–61.[74]

r This chapter was reviewed at the Consultative Meeting on Dengue Case Classification and Case Management held in Bangkok, Thailand, on 7–8 October 2010. The participants included experts from Member States of the WHO SEA and WP Regions and observers from the University of Massachusetts Medical School, USA and the Armed Forces Research Institute of Medical Sciences, Thailand. The Secretariat comprised staff from the WHO Collaborating Centre for Case Management of Dengue/DHF/DSS, QSNICH, Bangkok, Thailand.

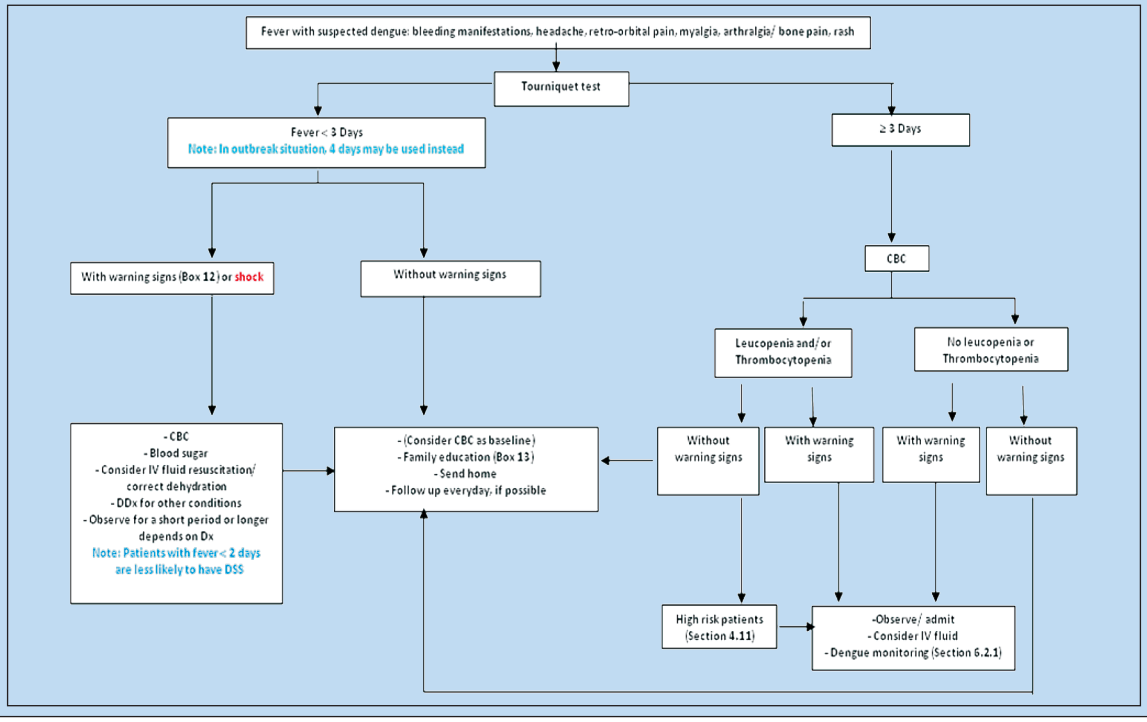
6.1 Triage of suspected dengue patients at OPD

During epidemics all hospitals, including those at the tertiary level, find a heavy influx of patients. Therefore, hospital authorities should organize a frontline "Dengue Desk" to screen and triage suspected dengue patients. Suggested triage pathways are indicated below in *Box 9* and *Box 10*.

Box 9: Steps for OPD screening during dengue outbreak



Box 10: Suggested triage pathway



Primary triage

Triage has to be performed by a trained and competent person.

- If the patient arrives in hospital in a severe/critical condition, then send this patient directly to a trained nurse/medical assistant (refer to number 3 below).
- For other patients, proceed as following:

  (1) History of the duration (number of days) of fever and warning signs (*Box 11*) of high-risk patients to be assessed by a trained nurse or staff, not necessarily medical.

  (2) Tourniquet test to be conducted by trained personnel (if there is not enough staff, just inflate the pressure to 80 mmHg for >12 years of age and 60 mmHg for children aged 5 to 12 years for five minutes).

  (3) Vital signs, including temperature, blood pressure, pulse rate, respiratory rate and peripheral perfusion, to be checked by trained nurse or medical assistant.

  Peripheral perfusion is assessed by palpation of pulse volume, temperature and colour of extremities, and capillary refill time. This is mandatory for all patients, particularly so when digital blood-pressure monitors and other machines are used. Particular attention is to be given to those patients who are afebrile and have tachycardia. These patients and those with reduced peripheral perfusion should be referred for immediate medical attention, CBC and blood sugar-level tests at the earliest possible.

  (4) Recommendations for CBC:

  – all febrile patients at the first visit to get the baseline HCT, WBC and PLT.
  – all patients with warning signs.
  – all patients with fever >3 days.
  – all patients with circulatory disturbance/shock (these patients should undergo a glucose check).

  Results of CBC: If leucopenia and/or thrombocytopenia is present, those with warning signs should be sent for immediate medical consultation.

  (5) Medical consultation: Immediate medical consultation is recommended for the following:

  – shock.
  – patients with warning signs, especially those whose illness lasts for >4 days.

  (6) Decision for observation and treatment:

  – Shock: Resuscitation and admission.
  – Hypoglycemic patients without leucopenia and/or thrombocytopenia should receive emergency glucose infusion and intravenous glucose containing fluids. Laboratory investigations should be done to determine the likely cause of illness. These patients should be observed for a period of 8–24 hours. Ensure clinical improvement before sending them home, and they should be monitored daily.
  – Those with warning signs.
  – High-risk patients with leucopenia and thrombocytopenia.

  (7) Patient and family advice should be carefully delivered before sending him/her home (*Box 12*). This can be done in a group of 5 to 20 patients by a trained person who may not be a nurse/doctor. Advice should include bed rest, intake of oral fluids or a soft diet, and reduction of fever by tepid sponging in addition to paracetamol. Warning signs should be emphasized, and it should be made clear that should these occur patients must seek *immediate* medical attention even if they have a scheduled appointment pending.

(8) Follow-up visits: Patients should be aware that the critical period is during the afebrile phase and that follow-up with CBC is essential to detect early danger signs such as leucopenia, thrombocytopenia, and/or haematocrit rise. Daily follow-up is recommended for all patients except those who have resumed normal activities or are normal when the temperature subsides.

Box 11: Warning signs

- No clinical improvement or worsening of the situation just before or during the transition to afebrile phase or as the disease progresses.
- Persistent vomiting, not drinking.
- Severe abdominal pain.
- Lethargy and/or restlessness, sudden behavioural changes.
- Bleeding: Epistaxis, black stool, haematemesis, excessive menstrual bleeding, dark-coloured urine (haemoglobinuria) or haematuria.
- Giddiness.
- Pale, cold and clammy hands and feet.
- Less/no urine output for 4–6 hours.

Box 12: Handout for home care of dengue patients (information to be given to patients and/or their family member(s) at the outpatient department)

A. Home care advice (family education) for patients:

- Patient needs to take adequate bed rest.
- Adequate intake of fluids (no plain water) such as milk, fruit juice, isotonic electrolyte solution, oral rehydration solution (ORS) and barley/rice water. Beware of over-hydration in infants and young children.
- Keep body temperature below 39 °C. If the temperature goes beyond 39 °C, give the patient paracetamol. Paracetamol is available in 325 mg or 500 mg doses in tablet form or in a concentration of 120 mg per 5 ml of syrup. The recommended dose is 10 mg/kg/dose and should be administered in frequencies of not less than six hours. The maximum dose for adults is 4 gm/day. Avoid using too much paracetamol, and *aspirin or NSAID is not recommended*.
- Tepid sponging of forehead, armpits and extremities. A lukewarm shower or bath is recommended for adults.

B. Watch out for the warning signs (as in *Box 11*):

- No clinical improvement or worsening of the situation just before or during the transition to afebrile phase or as the disease progresses.
- Persistent vomiting, lack of water intake.
- Severe abdominal pain.
- Lethargy and/or restlessness, sudden behavioural changes.
- Bleeding: Epistaxis, black coloured stools, haematemesis, excessive menstrual bleeding, dark-coloured urine (haemoglobinuria) or haematuria.
- Giddiness.
- Pale, cold and clammy hands and feet.
- Less/no urine output for 4–6 hours.

6.2 Management of DF/DHF cases in hospital observation wards/ on admission

The details of management of DF/DHF cases in hospital observation wards or upon admission are presented below:[75,76,77]

Monitoring of dengue/DHF patients during the critical period (thrombocytopenia around 100 000 cells/mm^3)

The critical period of DHF refers to the period of plasma leakage which starts around the time of defervescence or the transition from febrile to afebrile phase. Thrombocytopenia is a sensitive indicator of plasma leakage but may also be observed in patients with DF. A rising haematocrit of 10% above baseline is an early objective indicator of plasma leakage. Intravenous fluid therapy should be started in patients with poor oral intake or further increase in haematocrit and those with warning signs.

The following parameters should be monitored:

- General condition, appetite, vomiting, bleeding and other signs and symptoms.
- Peripheral perfusion can be performed as frequently as is indicated because it is an early indicator of shock and is easy and fast to perform.
- Vital signs such as temperature, pulse rate, respiratory rate and blood pressure should be checked at least every 2–4 hours in non-shock patients and 1–2 hours in shock patients.
- Serial haematocrit should be performed at least every four to six hours in stable cases and should be more frequent in unstable patients or those with suspected bleeding. It should be noted that haematocrit should be done before fluid resuscitation. If this is not possible, then it should be done after the fluid bolus but not during the infusion of the bolus.
- Urine output (amount of urine) should be recorded at least every 8 to 12 hours in uncomplicated cases and on an hourly basis in patients with profound/prolonged shock or those with fluid overload. During this period the amount of urine output should be about 0.5 ml/kg/h (this should be based on the ideal body weight).

Additional laboratory tests

Adult patients and those with obesity or suffering from diabetes mellitus should have a blood glucose test conducted. Patients with prolonged/profound shock and/or those with complications should undergo the laboratory investigations as shown in Box 13.

Correction of the abnormal laboratory results should be done: hypoglycemia, hypocalcemia and metabolic acidosis that do not respond to fluid resuscitation. Intravenous (IV) vitamin K1 may be administered during prolonged prothrombin time. It should be noted that in places where laboratory facilities are not available, calcium gluconate and vitamin K1 should be given in addition to intravenous therapy. In cases with profound shock and those not responding to IV fluid resuscitation, acidosis should be corrected with $NaHCO_3$ if pH is <7.35 and serum bicarbonate is <15 mEq/L.

Box 13: Additional laboratory investigations

- Complete blood count (CBC).
- Blood glucose.
- Blood gas analysis, lactate, if available.
- Serum electrolytes and BUN, creatinine.
- Serum calcium.
- Liver function tests.
- Coagulation profile, if available.
- Right lateral decubitus chest radiograph (optional).
- Group and match for fresh whole blood or fresh packed red cells.
- Cardiac enzymes or ECG if indicated, especially in adults.
- Serum amylase and ultrasound if abdominal pain does not resolve with fluid therapy.
- Any other test, if indicated.

Intravenous fluid therapy in DHF during the critical period

Indications for IV fluid:

- when the patient cannot have adequate oral fluid intake or is vomiting.
- when HCT continues to rise 10%–20% despite oral rehydration.
- impending shock/shock.

The general principles of fluid therapy in DHF include the following:

- ***Isotonic crystalloid solutions should be used throughout the critical period*** except in the very young infants <6 months of age in whom 0.45% sodium chloride may be used.
- Hyper-oncotic colloid solutions (osmolarity of >300 mOsm/l) such as dextran 40 or starch solutions may be used in patients with massive plasma leakage, and those not responding to the minimum volume of crystalloid (as recommended below). Iso-oncotic colloid solutions such as plasma and hemaccel may not be as effective.
- A volume of about maintenance +5% dehydration should be given to maintain a "just adequate" intravascular volume and circulation.
- The duration of intravenous fluid therapy should not exceed 24 to 48 hours for those with shock. However, for those patients who do not have shock, the duration of intravenous fluid therapy may have to be longer but not more than 60 to 72 hours. This is because the latter group of patients has just entered the plasma leakage period while shock patients have experienced a longer duration of plasma leakage before intravenous therapy is begun.
- In obese patients, the ideal body weight should be used as a guide to calculate the fluid volume (*Table 9*).

Table 9: Requirement of fluid based on ideal body weight

Ideal body weight (Kgs)	Maintenance (ml)	M +5% deficit (ml)	Ideal body weight (kgs)	Maintenance (ml)	M +5% deficit (ml)
5	500	750	35	1 800	3 550
10	1 000	1 500	40	1 900	3 900
15	1 250	2 000	45	2 000	4 250
20	1 500	2 500	50	2 100	4 600
25	1 600	2 850	55	2 200	4 950
30	1 700	3 200	60	2 300	5 300

Source: Holiday M.A., Segar W.E.. Maintenance need for water in parenteral fluid therapy. *Pediatrics* 1957;19: 823.[78]

- Rate of intravenous fluids should be adjusted to the clinical situation. The rate of IV fluid differs in adults and children. *Table 10* shows the comparable/equivalent rates of IV infusion in children and adults with respect to the maintenance.

Table 10: Rate of IV fluid in adults and children

Note	Children rate (ml/kg/hour)	Adult rate (ml/hour)
Half the maintenance M/2	1.5	40–50
Maintenance (M)	3	80–100
M + 5% deficit	5	100–120
M + 7% deficit	7	120–150
M + 10% deficit	10	300–500

Source: Holiday M.A., Segar W.E.. Maintenance need for water in parenteral fluid therapy. *Pediatrics* 1957; 19:823.[78]

- Platelet transfusion is not recommended for thrombocytopenia (no prophylaxis platelet transfusion). It may be considered in adults with underlying hypertension and very severe thrombocytopenia (less than 10 000 cell/mm^3).

Management of patients with warning signs

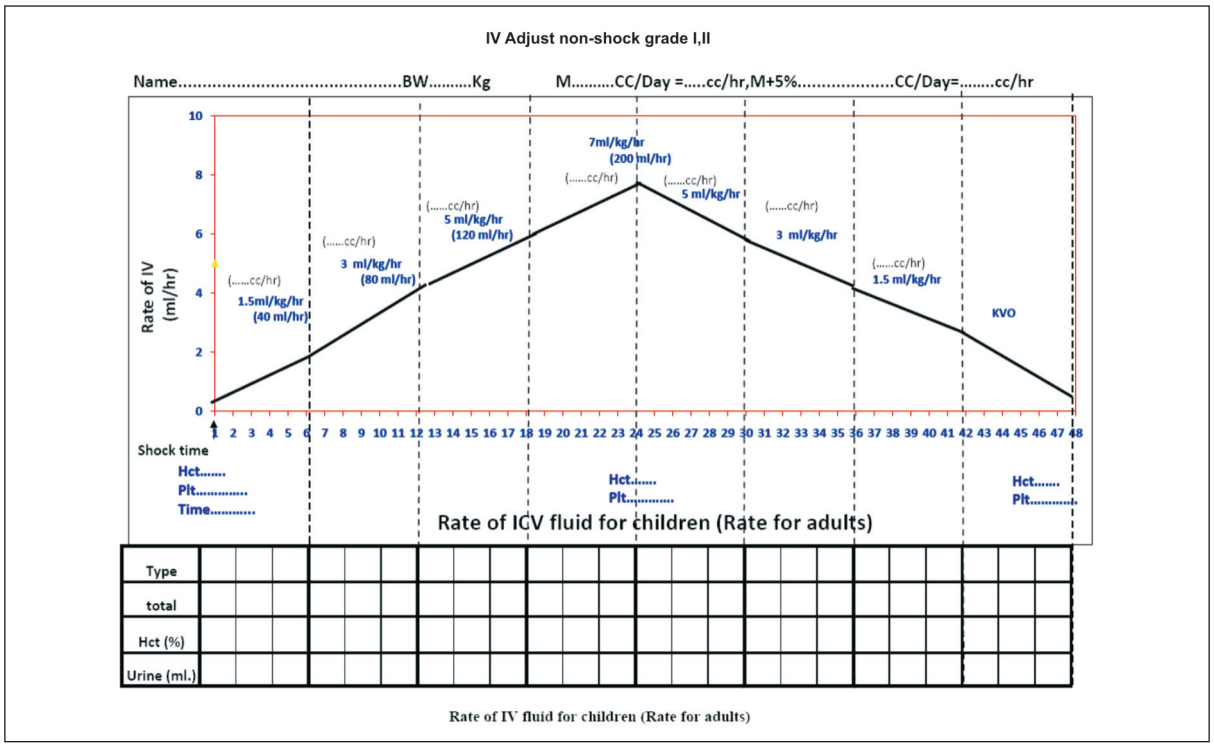
It is important to verify if the warning signs are due to dengue shock syndrome or other causes such as acute gastroenteritis, vasovagal reflex, hypoglycemia, etc. The presence of thrombocytopenia with evidence of plasma leakage such as rising haemotocrit and pleural effusion differentiates DHF/DSS from other causes. Blood glucose level and other laboratory tests may be indicated to find the causes. Management of DHF/DSS is detailed below. For other causes, IV fluids and supportive and symptomatic treatment should be given while these patients are under observation in hospital. They can be sent home within 8 to 24 hours if they show rapid recovery and are not in the critical period (i.e. when their platelet count is >100 000 cells/mm^3).

Management of DHF grade I, II (non-shock cases)

In general, the fluid allowance (oral + IV) is about maintenance (**for one day**) + 5% deficit (oral and IV fluid together), to be administered over **48** hours. For example, in a child weighing 20 kg, the deficit of 5% is 50 ml/kg x 20 = **1000 ml**. The maintenance is **1500 ml for one day**. Hence, the total of M + 5% is **2500 ml** (*Figure 8*). This volume is to be administered over **48 hours in non-shock patients**. The rate of infusion of this 2500 ml may be as shown in *Figure 8* below [please

note that the rate of plasma leakage is NOT even]. The rate of IV replacement should be adjusted according to the rate of plasma loss, guided by the clinical condition, vital signs, urine output and haematocrit levels.

Figure 8: Rate of infusion in non-shock cases



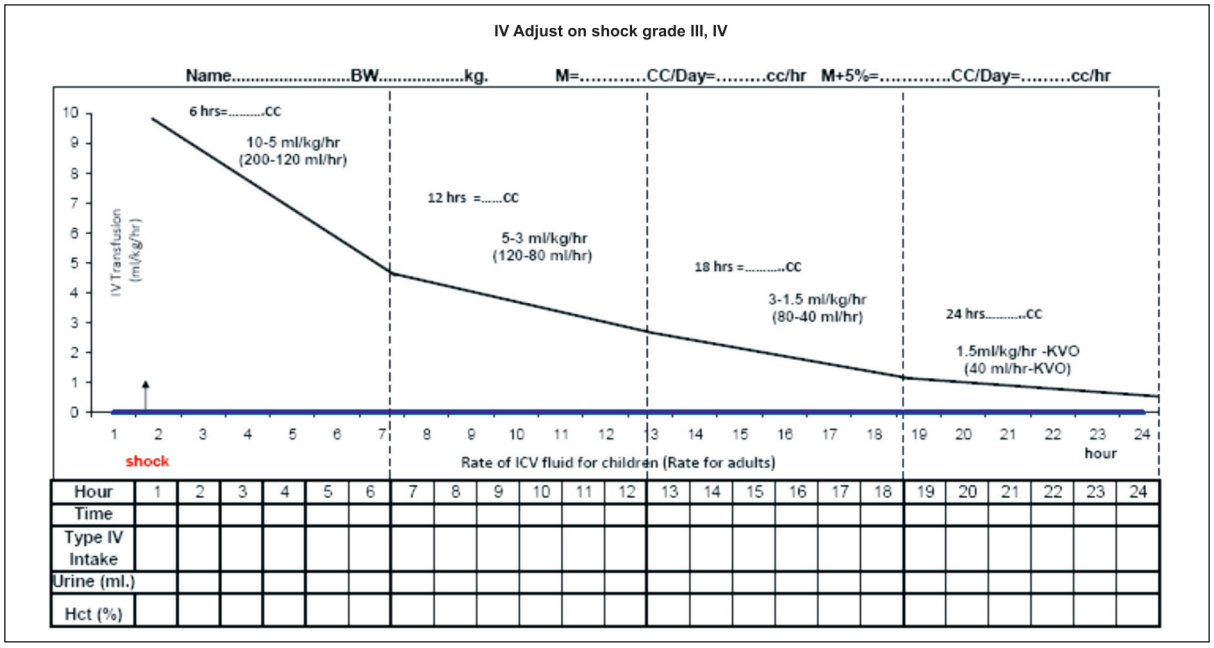
Source: Kalayanarooj S. and Nimmannitya S. In: Guidelines for Dengue and Dengue Haemorrhagic Fever Management. Bangkok Medical Publisher, Bangkok 2003.[79]

Management of shock: DHF Grade 3

DSS is hypovolemic shock caused by plasma leakage and characterized by increased systemic vascular resistance, manifested by narrowed pulse pressure (systolic pressure is maintained with increased diastolic pressure, e.g. 100/90 mmHg). When ***hypotension*** is present, one should suspect that severe ***bleeding, and often concealed gastrointestinal bleeding***, may have occurred in addition to the plasma leakage.

It should be noted that the fluid resuscitation of DSS is different from other types of shock such as septic shock. Most cases of DSS will respond to 10 ml/kg in children or 300–500 ml in adults over one hour or by bolus, if necessary. Further, fluid administration should follow the graph as in *Figure 9*. However, before reducing the rate of IV replacement, the clinical condition, vital signs, urine output and haematocrit levels should be checked to ensure clinical improvement.

Figure 9: Rate of infusion in DSS case



Source: Kalayanarooj S. and Nimmannitya S. In: Guidelines for Dengue and Dengue Haemorrhagic Fever Management. Bangkok Medical Publisher, Bangkok 2003.[79]

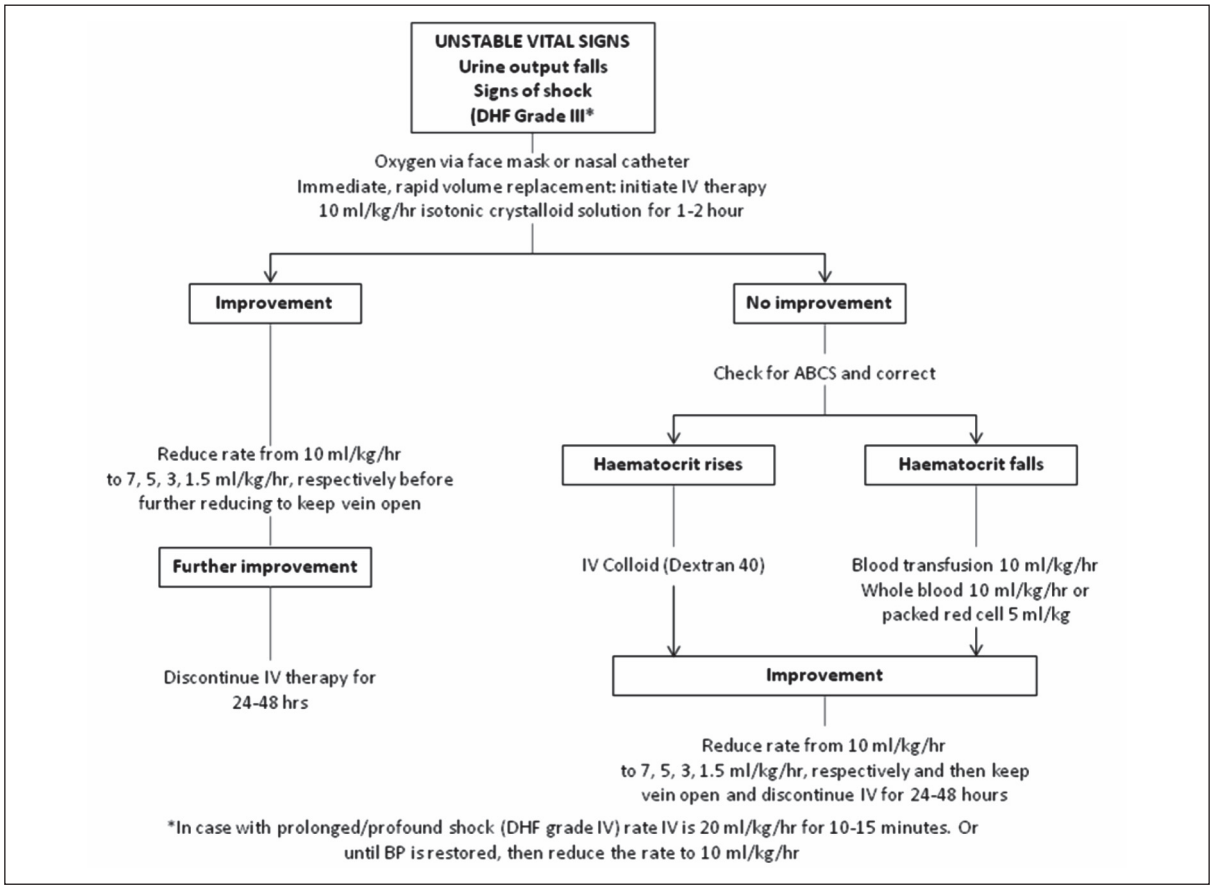
Laboratory investigations (ABCS) should be carried out in both shock and non-shock cases when no improvement is registered in spite of adequate volume replacement (*Box 14*).

Box 14: Laboratory investigations (ABCS) for patients who present with profound shock or have complications, and in cases with no clinical improvement in spite of adequate volume replacement

Abbreviation	Laboratory investigations	Note
A—Acidosis	Blood gas (capillary or venous)	Indicate prolonged shock. Organ involvement should also be looked into; liver function and BUN, creatinine.
B—Bleeding	Haematocrit	If dropped in comparison with the previous value or not rising, cross-match for rapid blood transfusion.
C—Calcium	Electrolyte, Ca++	Hypocalcemia is found in almost all cases of DHF but asymptomatic. Ca supplement in more severe/ complicated cases is indicated. The dosage is 1 ml/kg, dilute two times, IV push slowly (and may be repeated every six hours, if needed), maximum dose 10 ml of Ca gluconate.
S—Blood sugar	Blood sugar (dextrostix)	Most severe DHF cases have poor appetite together with vomiting. Those with impaired liver function may have hypoglycemia. Some cases may have hyperglycemia.

It is essential that the rate of IV fluid be reduced as peripheral perfusion improves; but it must be continued for a minimum duration of 24 hours and discontinued by 36 to 48 hours. Excessive fluids will cause massive effusions due to the increased capillary permeability. The volume replacement flow for patients with DSS is illustrated below (*Box 15*).

Box 15: Volume replacement flow chart for patients with DSS[s]



Management of prolonged/profound shock: DHF Grade 4

The initial fluid resuscitation in Grade 4 DHF is more vigorous in order to quickly restore the blood pressure and laboratory investigations should be done as soon as possible for ABCS as well as organ involvement. Even mild hypotension should be treated aggressively. ***Ten ml/kg of bolus fluid should be given as fast as possible, ideally within 10 to 15 minutes.*** When the blood pressure is restored, further intravenous fluid may be given as in Grade 3. ***If shock is not reversible after the first 10 ml/kg, a repeat bolus of 10 ml/kg and laboratory results should be pursued and corrected as soon as possible.*** Urgent blood transfusion should be considered as the next step (after reviewing the pre-resuscitation HCT) and followed up by closer monitoring, e.g. continuous bladder catheterization, central venous catheterization or arterial lines.

It should be noted that restoring the blood pressure is critical for survival and if this cannot be achieved quickly then the prognosis is extremely grave. Inotropes may be used to support the blood pressure, if volume replacement has been considered to be adequate such as in high central venous pressure (CVP), or cardiomegaly, or in documented poor cardiac contractility.

s Modified from Nimmannitya, S. In: Comprehensive Guidelines for Dengue and Dengue Haemorrahgic Fever, WHO SEAR Publication 1999.

If blood pressure is restored after fluid resuscitation with or without blood transfusion, and organ impairment is present, the patient has to be managed appropriately with special supportive treatment. Examples of organ support are peritoneal dialysis, continuous renal replacement therapy and mechanical ventilation.

If intravenous access cannot be obtained urgently, try oral electrolyte solution if the patient is conscious or the intraosseous route if otherwise. The intraosseous access is life-saving and should be attempted after 2–5 minutes or after two failed attempts at peripheral venous access or after the oral route fails.

Management of severe haemorrhage

- If the source of bleeding is identified, attempts should be made to stop the bleeding if possible. Severe epistaxis, for example, may be controlled by nasal packing. Urgent blood transfusion is life-saving and should not be delayed till the HCT drops to low levels. If blood loss can be quantified, this should be replaced. However, if this cannot be quantified, aliquots of 10 ml/kg of fresh whole blood or 5 ml/kg of freshly packed red cells should be transfused and response evaluated. The patient may require one or more aliquot.
- In gastrointestinal bleeding, H-2 antagonists and proton pump inhibitors have been used, but there has been no proper study to show its efficacy.
- There is no evidence to support the use of blood components such as platelet concentrates, fresh frozen plasma or cryoprecipitate. Its use could contribute to fluid overload.
- Recombinant Factor 7 might be helpful in some patients without organ failure, but it is very expensive and generally not available.

Management of high-risk patients

- Obese patients have less respiratory reserves and care should be taken to avoid excessive intravenous fluid infusions. The ideal body weight should be used to calculate fluid resuscitation and replacement and colloids should be considered in the early stages of fluid therapy. Once stabilized, furosemide may be given to induce diuresis.
- Infants also have less respiratory reserves and are more susceptible to liver impairment and electrolyte imbalance. They may have a shorter duration of plasma leakage and usually respond quickly to fluid resuscitation. Infants should, therefore, be evaluated more frequently for oral fluid intake and urine output.
- Intravenous insulin is usually required to control the blood sugar levels in dengue patients with diabetes mellitus. Non-glucose containing crystalloids should be used.
- Pregnant women with dengue should be admitted early to intensely monitor disease progress. Joint care among obstetrics, medicine and paediatrics specialities is essential. Families may have to be counselled in some severe situations. Amount and rate of IV fluid for pregnant women should be similar to those for non-pregnant woman using pre-pregnant weight for calculation.
- Patients with hypertension may be on anti-hypertensive therapy that masks the cardiovascular response in shock. The patient's own baseline blood pressure should be considered. A blood pressure that is perceived to be normal may in fact be low for these patients.
- Anti-coagulant therapy may have to be stopped temporarily during the critical period.
- Haemolytic diseases and haemoglobinopathies: These patients are at risk of haemolysis and will require blood transfusion. Caution should accompany hyperhydration and alkalinization therapy, which can cause fluid overload and hypocalcemia.

- Congenital and ischaemic heart diseases: Fluid therapy should be more cautious as they may have less cardiac reserves.
- For patients on steroid therapy, continued steroid treatment is recommended but the route may be changed.

Management of convalescence

- Convalescence can be recognized by the improvement in clinical parameters, appetite and general well-being.
- Haemodynamic state such as good peripheral perfusion and stable vital signs should be observed.
- Decrease of HCT to baseline or below and dieresis are usually observed.
- **Intravenous fluid should be discontinued.**
- In those patients with massive effusion and ascites, hypervolemia may occur and diuretic therapy may be necessary to prevent pulmonary oedema.
- Hypokalemia may be present due to stress and diuresis and should be corrected with potassium-rich fruits or supplements.
- Bradycardia is commonly found and requires intense monitoring for possible rare complications such as heart block or ventricular premature contraction (VPC).
- Convalescence rash is found in 20%–30% of patients.

Signs of recovery

- Stable pulse, blood pressure and breathing rate.
- Normal temperature.
- No evidence of external or internal bleeding.
- Return of appetite.
- No vomiting, no abdominal pain.
- Good urinary output.
- Stable haematocrit at baseline level.
- Convalescent confluent petechiae rash or itching, especially on the extremities.

Criteria for discharging patients

- Absence of fever for at least 24 hours without the use of anti-fever therapy.
- Return of appetite.
- Visible clinical improvement.
- Satisfactory urine output.
- A minimum of 2–3 days have elapsed after recovery from shock.
- No respiratory distress from pleural effusion and no ascites.
- Platelet count of more than 50 000/mm^3. If not, patients can be recommended to avoid traumatic activities for at least 1–2 weeks for platelet count to become normal. In most uncomplicated cases, platelet rises to normal within 3–5 days.

Management of complications

The most common complication is fluid overload.

Detection of fluid overload in patients

- Early signs and symptoms include puffy eyelids, distended abdomen (ascites), tachypnoea, mild dyspnoea.
- Late signs and symptoms include all of the above, along with moderate to severe respiratory distress, shortness of breath and wheezing (not due to asthma) which are also an early sign of interstitial pulmonary oedema and crepitations. Restlessness/agitation and confusion are signs of hypoxia and impending respiratory failure.

Management of fluid overload

Review the total intravenous fluid therapy and clinical course, and check and correct for ABCS (Box 14). All hypotonic solutions should be stopped.

In the early stage of fluid overload, switch from crystalloid to colloid solutions as bolus fluids. Dextran 40 is effective as 10 ml/kg bolus infusions, but the dose is restricted to 30 ml/kg/day because of its renal effects. Dextran 40 is excreted in the urine and will affect urine osmolarity. Patients may experience "sticky" urine because of the hyperoncotic nature of Dextran 40 molecules (osmolarity about twice that of plasma). Voluven may be effective (osmolarity = 308 mosmole) and the upper limit is 50ml/kg/day. However, no studies have been done to prove its effectiveness in cases of DHF/DSS.

In the late stage of fluid overload or those with frank pulmonary oedema, furosemide may be administered if the patient has stable vital signs. If they are in shock, together with fluid overload 10 ml/kg/h of colloid (dextran) should be given. When the blood pressure is stable, usually within 10 to 30 minutes of infusion, administer IV 1 mg/kg/dose of furosemide and continue with dextran infusion until completion. Intravenous fluid should be reduced to as low as 1 ml/kg/h until discontinuation when haematocrit decreases to baseline or below (with clinical improvement). The following points should be noted:

- These patients should have a urinary bladder catheter to monitor hourly urine output.
- Furosemide should be administered during dextran infusion because the hyperoncotic nature of dextran will maintain the intravascular volume while furosemide depletes in the intravascular compartment.
- **After administration of furosemide, the vital signs should be monitored every 15 minutes for one hour to note its effects.**
- If there is no urine output in response to furosemide, check the intravascular volume status (CVP or lactate). If this is adequate, pre-renal failure is excluded, implying that the patient is in an acute renal failure state. These patients may require ventilatory support soon. If the intravascular volume is inadequate or the blood pressure is unstable, check the ABCS (Box 14) and other electrolyte imbalances.
- In cases with no response to furosemide (no urine obtained), repeated doses of furosemide and doubling of the dose are recommended. If oliguric renal failure is established, renal replacement therapy is to be done as soon as possible. These cases have poor prognosis.
- Pleural and/or abdominal tapping may be indicated and can be life-saving in cases with severe respiratory distress and failure of the above management. This has to be done with extreme caution because traumatic bleeding is the most serious complication and leads to death. Discussions and explanations about the complications and the prognosis with families are mandatory before performing this procedure.

Management of encephalopathy

Some DF/DHF patients present unusual manifestations with signs and symptoms of central nervous system (CNS) involvement, such as convulsion and/or coma. This has generally been shown to be

encephalopathy, not encephalitis, which may be a result of intracranial haemorrhage or occlusion associated with DIC or hyponatremia. In recent years, there has been an increasing number of reported cases with CNS infections documented by virus isolations from the cerebrospinal fluid (CSF) or brain.

Most of the patients with encephalopathy report hepatic encephalopathy. The principal treatment of hepatic encephalopathy is to prevent the increase of intracranial pressure (ICP). Radiological imaging of the brain (CT scan or MRI) is recommended if available to rule out intracranial haemorrhage. The following are recommendations for supportive therapy for this condition:

- Maintain adequate airway oxygenation with oxygen therapy. Prevent/reduce ICP by the following measures:
  - give minimal IV fluid to maintain adequate intravascular volume; ideally the total IV fluid should not be >80% fluid maintenance.
  - switch to colloidal solution earlier if haematocrit continues to rise and a large volume of IV is needed in cases with severe plasma leakage.
  - administer a diuretic if indicated in cases with signs and symptoms of fluid overload.
  - positioning of the patient must be with the head up by 30 degrees.
  - early intubation to avoid hypercarbia and to protect the airway.
  - may consider steroid to reduce ICP. Dexamethazone 0.15 mg/kg/dose IV to be administered every 6–8 hours.
- Decrease ammonia production by the following measures:
  - give lactulose 5–10 ml every six hours for induction of osmotic diarrhoea.
  - local antibiotic gets rid of bowel flora; it is not necessary if systemic antibiotics are given.
- Maintain blood sugar level at 80–100 mg/dl per cent. Recommend glucose infusion rate is anywhere between 4–6 mg/kg/hour.
- Correct acid-base and electrolyte imbalance, e.g. correct hypo/hypernatremia, hypo/hyperkalemia, hypocalcemia and acidosis.
- Vitamin K1 IV administration; 3 mg for <1-year-old, 5 mg for <5-year-old and 10 mg for>5-year-old and adult patients.
- Anticonvulsants should be given for control of seizures: phenobarbital, dilantin and diazepam IV as indicated.
- Transfuse blood, preferably freshly packed red cells, as indicated. Other blood components such as as platelets and fresh frozen plasma may not be given because the fluid overload may cause increased ICP.
- Empiric antibiotic therapy may be indicated if there are suspected superimposed bacterial infections.
- H2-blockers or proton pump inhibitor may be given to alleviate gastrointestinal bleeding.
- Avoid unnecessary drugs because most drugs have to be metabolized by the liver.
- Consider plasmapheresis or haemodialysis or renal replacement therapy in cases with clinical deterioration.

Referral and transportation

More severe/complicated cases should be managed in hospitals where almost all laboratory investigations, equipment, medicines and blood bank facilities are available. The medical and nursing personnel may be

more experienced in the care of these critically ill dengue patients. The following patients should be referred for closer monitoring and probably accorded special treatment at a higher tier of hospital care:

- infants <1 year old.
- obese patients.
- pregnant women.
- profound/prolonged shock.
- significant bleeding.
- repeated shock 2–3 times during treatment.
- patients who seem not to respond to conventional fluid therapy.
- patients who continue to have rising haematocrit and no colloidal solution is available.
- patients with known underlying diseases such as Diabetes mellitus (DM) , hypertension, heart disease or haemolytic disease.
- patients with signs and symptoms of fluid overload.
- patient with isolated/multiple organ involvement.
- patients with neurological manifestations such as change of consciousness, semi-coma, coma, convulsion, etc.

Referral procedure

- Discussions and counselling sessions with families.
- Prior contact with the referral hospital; communicating with doctors and nurses responsible.
- Stabilizing patients before transfer.
- Ensuring that the referral letter must contain information about clinical conditions, monitoring parameters (haematocrit, vital signs, intake/output), and progression of disease including all important laboratory findings.
- Taking care during transportation. Rate of IV fluid is important during this time. It is preferable to be given at a slower rate of about 5 ml/kg/h to prevent fluid overload. At least a nurse should accompany the patient.
- Review of referred patients by a specialist as soon as they arrive at the referral hospital.

Outbreak preparedness for clinical management

There has been increasing incidence of dengue outbreaks in many countries globally. The following elements are recommended for the preparedness of dengue clinical management:

- Organization of a rapid response team coordinated by the national programme:
  - frontline health-care centre.
  - emergency department.
  - medical team.
  - laboratory team.
  - epidemiology team.
- Personnel (to be recruited, trained and assigned appropriate duties):
  - doctors.
  - nurses.
  - health-care workers.
  - back-office personnel.

- *Clinical Practice Guidelines* (CPG) (the above-named personnel should undergo a brief training on the use of CPG).
- Medicines and solutions:
  - paracetamol.
  - oral rehydration solution.
  - IV fluid.
    - crystalloid: 0.9% and 5% Dextrose in isotonic normal saline solution (D/NSS), 5% Dextrose Aectated Ringer's (DAR), 5% Dextrose Lactated Ringer's (DLR).
    - colloid-hyperoncotic (plasma expander): 10% dextran–40 in NSS.
  - 20% or 50% glucose.
  - vitamin K1.
  - calcium gluconate.
  - potassium Chloride (KCl) solution.
  - sodium bicarbonate.
- Equipment and supplies:
  - IV fluids and vascular access, including scalp vein, medicut, cotton, gauze and 70% alcohol.
  - oxygen and delivery systems.
  - sphygmomanometer with three different cuff sizes.
  - automate CBC machine (Coulter counter).
  - micro-centrifuge (for haematocrit determination).
  - microscope (for platelet count estimation).
  - glucometer (for blood-sugar level).
  - lactatemeter.
- Laboratory support:
  - Basic:
    - Complete blood count (CBC): haematocrit, white blood cell (WBC) count, platelet count and differential count.
  - More complicated cases:
    - blood sugar.
    - liver function test.
    - renal function test (BUN, creatinine).
    - electrolyte, calcium.
    - blood gas analysis.
    - coagulogram: partial thromboplastin time (PTT), prothrombin time (PT), thrombin time (TT).
    - chest X-ray.
    - ultrasonography.
- Blood bank:
  - fresh whole blood, packed red cell (platelet concentrate).

7. Disease Surveillance: Epidemiological and Entomological

7.1 Epidemiological surveillance

Epidemiological surveillance is an ongoing systematic collection, recording, analysis, interpretation and dissemination of data for initiating suitable public health interventions for prevention and control.

Objectives of surveillance

The objectives of public health surveillance applicable to dengue are to:

- detect epidemics early for timely intervention;
- measure the disease burden;
- monitor trends in the distribution and spread of dengue over time;
- assess the social and economic impact of dengue on the affected community;
- evaluate the effectiveness of prevention and control programmes; and
- facilitate planning and resource allocation based on the lessons learnt from programme evaluation.

Components of a surveillance system

The surveillance system comprises passive surveillance, active surveillance and event-based surveillance.

All three surveillance components require a good public health laboratory to provide diagnostic support in virology, bacteriology and parasitology. The laboratory need not be able to test for all agents but should know where to refer specimens for testing, for example, select samples for the WHO collaborating centres for reference and research.

Individually, the three components are not sensitive enough to provide effective early warning. But when used collectively they can often accurately predict epidemic activity.

Passive surveillance

Every dengue endemic country should have a surveillance system and it should be mandated by law in most countries that DF/DHF is treated as a reportable disease. The system should be based on standardized case definitions (*Box 8 on pages 29–30*) and formalized mandated reporting. Although passive systems are not sensitive and have low specificity since cases are not laboratory confirmed, they are most useful in monitoring long-term trends in dengue transmission.

The clinical spectrum of illnesses associated with dengue infection ranges from non-specific viral syndrome to severe haemorrhagic disease or fatal shock. It may sometimes be difficult to

differentiate the associated illnesses from those caused by other viruses, bacteria and parasites. Therefore, surveillance should be supported by laboratory diagnosis. However, the reporting of dengue disease generally has to rely on clinical diagnosis combined with simple clinical laboratory tests and available epidemiological information.

Passive surveillance should require case reports from every clinic, private physician and health centre or hospital that provides medical attention to the population at risk. However, even when mandated by law, 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 low. Moreover, many patients with mild, non-specific viral syndrome self medicate at home and do not seek formal treatment. By the time dengue cases are detected and reported by physicians under a passive surveillance system, substantial transmission has already occurred and it may even have peaked. In such cases, it is often too late to control the epidemic.

However, passive surveillance for DF/DHF has two problems. First, there is no consistency in reporting standards. Some countries report only DHF while others report both DF and DHF. Secondly, the WHO case definitions are also not strictly adhered to while reporting the cases. These problems lead to both underreporting and overreporting that actually weakens the surveillance systems.

Active surveillance

The goals of an active surveillance system allow health authorities to monitor dengue transmission in a community and tell, at any point in time, where transmission is occurring, which virus serotypes are circulating, and what kind of illness is associated with the dengue infection.[4] To accomplish this, the system must be active and have good diagnostic laboratory support. Effectively managed, such a surveillance system should be able to provide an early warning or predictive capability for epidemic transmission. The rationale is that if epidemics can be predicted, they can be prevented. This type of proactive surveillance system must have at least three components that place emphasis on the inter- or pre-epidemic period. These are a sentinel clinic/physician network, a fever alert system that uses community health workers, and a sentinel hospital system (*Box 16*).

Box 16: Components of laboratory-based, proactive surveillance for DF/DHF during inter-epidemic periods[t]

Type of surveillance	Samples[u]	Approach
Sentinel clinic/physician	Blood from representative cases of viral syndrome, taken 5 to 15 days after the onset of symptoms.	Representative samples taken round the year and processed timely for virus isolation and for IgM antibodies.
Fever alert	Blood samples from representative cases of febrile illness.	Increased febrile illness in the community is investigated immediately.
Sentinel hospital	Blood and tissue samples taken during hospitalization and/or at the time of death.	All haemorrhagic disease and all viral syndromes with fatal outcome are investigated immediately.

t During an epidemic, after the virus serotype(s) is known, the case definition should be more specific and surveillance focused on severe disease.

u All samples are processed weekly for virus isolation and/or for dengue-specific IgM antibodies.

The sentinel clinic/physician and fever alert components are designed to monitor non-specific viral syndromes in the community. This is especially important for dengue viruses because they are frequently maintained in tropical urban centres in a silent transmission cycle, often presenting as non-specific viral syndromes. The sentinel clinic/physician and fever alert systems are also very useful for monitoring other common infectious diseases such as influenza, measles, malaria, typhoid, leptospirosis and others that present in the acute phase as non-specific febrile illnesses.

In contrast to the sentinel clinic/physician component, which requires sentinel sites to monitor routine viral syndromes, the fever alert system relies on community health and sanitation and the alertness of other workers to any increase in febrile activity in their community, and to report this to the health department's central epidemiology unit. Investigations by the latter should be immediate but flexible. It may involve telephonic follow-up or active investigation by an epidemiologist who visits the area to take samples.

The sentinel hospital component should be designed to monitor severe disease. Hospitals used as sentinel sites should include all facilities that admit patients for severe infectious diseases in the community. This network should also include the physicians for infectious disease who usually consult patients with such cases. The system can target any type of severe disease, but for dengue it should include all patients with any haemorrhagic manifestation; an admission diagnosis of viral encephalitis, aseptic meningitis and meningococcal shock; and/or a fatal outcome following a viral prodrome.[19]

An active surveillance system is designed to monitor disease activity during the inter-epidemic period prior to increased transmission. *Box 16* outlines the active surveillance system for DF/DHF, giving the types of specimens and approaches required. **It must be emphasized that once epidemic transmission has begun, the active surveillance system must be refocused on severe disease rather than on viral syndromes. Surveillance systems should be designed and adapted to the areas where they will be initiated.**

Event-based surveillance

Event-based surveillance is aimed at investigating an unusual health event, namely fevers of unknown aetiology and clustering of cases. Unlike the classical surveillance system, event-based surveillance is not based on routine collection of data but should be an investigation conducted by an epidemiological unit – supported by a microbiologist, an entomologist and other personnel relevant to the particular event – to initiate interventions to control and prevent further spread of the infection.

7.2 International Health Regulations (2005)

The International Health Regulations (IHR) were formulated in 2005 (World Health Assembly resolution WHA58.3) and came into force in 2007. The purpose and scope of these Regulations are to prevent, protect against, control and provide a public health response to the international spread of disease in ways that are commensurate with and restricted to public health risks, and which avoid unnecessary interference with international traffic and trade.[2]

The IHR (2005) encompass dengue as a disease of concern to the international community because of its high potential for build-up of epidemics of DF and DHF. The IHR enjoin Member States to develop capabilities for detection, reporting and responding to global health threats by establishing effective surveillance systems. Core obligations for Member States and for WHO are outlined in the Decision Instrument for the assessment and notification of events that may constitute a public health emergency of international concern (PHEIC). These are also mentioned in Annex 2

and 3 respectively. Thailand is the first country in the South-East Asia Region to have developed an IHR Action Plan for 2008–2012 (*Box 17*).

Box 17: Thailand develops IHR Action Plan for 2008–2012[80]

The Ministry of Public Health, Royal Government of Thailand, has formulated national action plans to develop public health infrastructure and human resources to meet the core capacity requirements as envisaged under the International Health Regulations (2005). The Plan for 2008–2012 was approved by the Cabinet in December 2007. The objectives of the Plan focus on capacity-building of all institutions involved in surveillance and public health emergencies, including laboratories and hospitals, and the 18 points of entry, and also on building capacity to coordinate, among various related governmental and private institutions and the community, the implementation of IHR (2005) in an integrated manner.

7.3 Vector surveillance

Surveillance of *Ae. aegypti* is important in determining the distribution, population density, major larval habitats, and spatial and temporal risk factors related to dengue transmission, and levels of insecticide susceptibility or resistance,[81] in order to prioritize areas and seasons for vector control. These data will enable the selection and use of the most appropriate vector control tools, and can be used to monitor their effectiveness. There are several methods available for the detection and monitoring of larval and adult populations. The selection of appropriate methods depends on surveillance objectives, levels of infestation, and availability of resources.

Larval surveys

For practical reasons, the most common survey methodologies employ larval sampling procedures rather than egg or adult collections. The basic sampling unit is the house or premise, which is systematically searched for water-storage containers.

Containers are examined for the presence of mosquito larvae and pupae. Depending on the objectives of the survey, the search may be terminated as soon as *Aedes* larvae are found, or it may be continued until all containers have been examined. The collection of specimens for laboratory examination is necessary to confirm the species present. Three commonly used indices for monitoring *Ae. aegypti* infestation levels[81,82] are presented in *Box 18*.

Box 18: Indices used to assess the levels of Ae. aegypti infestations

House Index (HI): Percentage of houses infested with larvae and/or pupae.

$$HI = \frac{\text{Number of houses infested}}{\text{Number of houses inspected}} \times 100$$

Container Index (CI): Percentage of water-holding containers infested with larvae or pupae.

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

Breateau Index (BI): Number of positive containers per 100 houses inspected.

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

The House Index has been most widely used for monitoring infestation levels, but it neither takes 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 Breateau Index establishes a relationship between positive containers and houses, and is considered to be the most informative, but again there is no reflection of container productivity. Nevertheless, in the course of gathering basic information for calculating the Breateau Index, it is possible and 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 tyres per 100 houses, etc.). These data are particularly relevant to focus efforts for the management or elimination of the most common habitats and for the orientation of educational messages in aid of community-based initiatives.

Pupal/demographic surveys

The rate of contribution of newly emerged adults to the adult mosquito population from different container types can vary widely. The estimates of relative adult production may be based on pupal counts[81] (i.e. counting all pupae found in each container). The corresponding index is the Pupal Index (*Box 19*).

Box 19: Pupal Index: Number of pupae per house

$$\text{Pupal Index (PI)} = \frac{\text{Number of pupae}}{\text{Number of houses inspected}} \times 100$$

In order to compare the relative importance of larval habitats, the Pupal Index can be disaggregated by "useful", "non-essential" and "natural" containers, or by specific habitat types such as tyres, flower vases, drums, clay pots, etc. Given the practical difficulties faced and labour-intensive efforts entailed in obtaining pupal counts, especially from large containers, this method may not be used for routine monitoring or in every survey of *Ae. aegypti* populations, but may be reserved for

special studies or used in each locality once during the wet season and once during the dry season to determine the most productive container types. The Pupal Index has been most frequently used for operational research purposes.

In any community, if the classes of containers with the highest rates of adult emergence are known, their selective targeting for source reduction or other vector control interventions can be the basis for the optimized use of limited resources.[83,84] The pupal/demographic survey is a method for identifying these epidemiologically most important container classes. Unlike the traditional indices described above, pupal/demographic surveys measure the total number of pupae in different classes of containers in a given community.

In practice, conducting a pupal/demographic survey involves visiting a sampling of houses. The number of persons living in the house is recorded. At each location, and with the permission of the householder, the field workers systematically search for and strain the contents of each water-filled container through a sieve, and re-suspend the sieved contents in a small amount of clean water in a white enamel or plastic pan. All the pupae are pipetted into a labelled vial. Large containers are a significant problem in pupal/demographic surveys because of the difficulty of determining the absolute number of pupae. In such circumstances sweep-net methods have been developed with calibration factors to estimate the total number of pupae in specific container types. If there is container-inhabiting species in the area other than *Ae. aegypti*, on return to the laboratory the contents of each vial are transferred to small cups and covered with mosquito netting secured with a rubber band. They are held until adult emergence occurs and taxonomic identification and counts can be made.

The collection of demographic data makes it possible to calculate the ratio between the numbers of pupae (a proxy for adult mosquitoes) and persons in the community. There is growing evidence to suggest that together with other epidemiological parameters, notably dengue serotype-specific seroconversion rates and temperature, it is possible to determine the degree of vector control needed in a specific location to inhibit virus transmission. This remains an important area for research and awaits validation.

Adult surveys

Adult vector sampling procedures can provide valuable data for specific studies such as seasonal population trends, transmission dynamics, transmission risk, and evaluation of adulticide interventions. However, the results may be less reproducible than those obtained from the sampling of immature stages. The collection methods also tend to be labour-intensive and heavily dependent on the proficiency and skill of the collector.

Landing collections

Landing collections on humans are a sensitive means of detecting low-level infestations, but are very labour-intensive. Both male and female *Ae. Aegypti* are attracted to humans. Since adult males have low dispersal rates, their presence can be a reliable indicator of proximity to hidden larval habitats. The rates of capture, typically using hand nets or aspirators as mosquitoes approach or land on the collector, are usually expressed in terms of "landing counts per man hour". As there is no prophylaxis for dengue or other viruses transmitted by *Aedes* mosquitoes, the method raises safety and ethical concerns in endemic areas.

Resting collections

During periods of inactivity, adult mosquitoes typically rest indoors, especially in bedrooms, and mostly in dark places such as clothes closets and other sheltered sites. Resting collections require systematic

searching of these sites for adult mosquitoes with the aid of a flashlight. A labour-intensive method is to capture the adults using mouth or battery-powered aspirators and hand-held nets with the aid of flashlights. Recently, a much more productive, standardized and less labour-intensive method using battery-operated backpack aspirators has been developed.[85] Following a standardized, timed collection routine in select rooms of each house, densities are recorded as the number of adults collected per house (females, males or both) or the number of adults collected for every human-hour of effort. When the mosquito population density is low, the percentage of houses found positive for adults is sometimes used.

Another means of collecting adult mosqutoes is through the use of the insecticide impregnated fabric trap[86,87] (IIFT), wherein the mosquitoes resting on the fabric hung inside the trap get killed upon contact with the insecticide and are collected in the bottom tray of the trap. These can then be sorted according to species and checked for the presence of *Aedes*. These traps, however, need to be evaluated for their efficacy in different field settings.

Oviposition traps

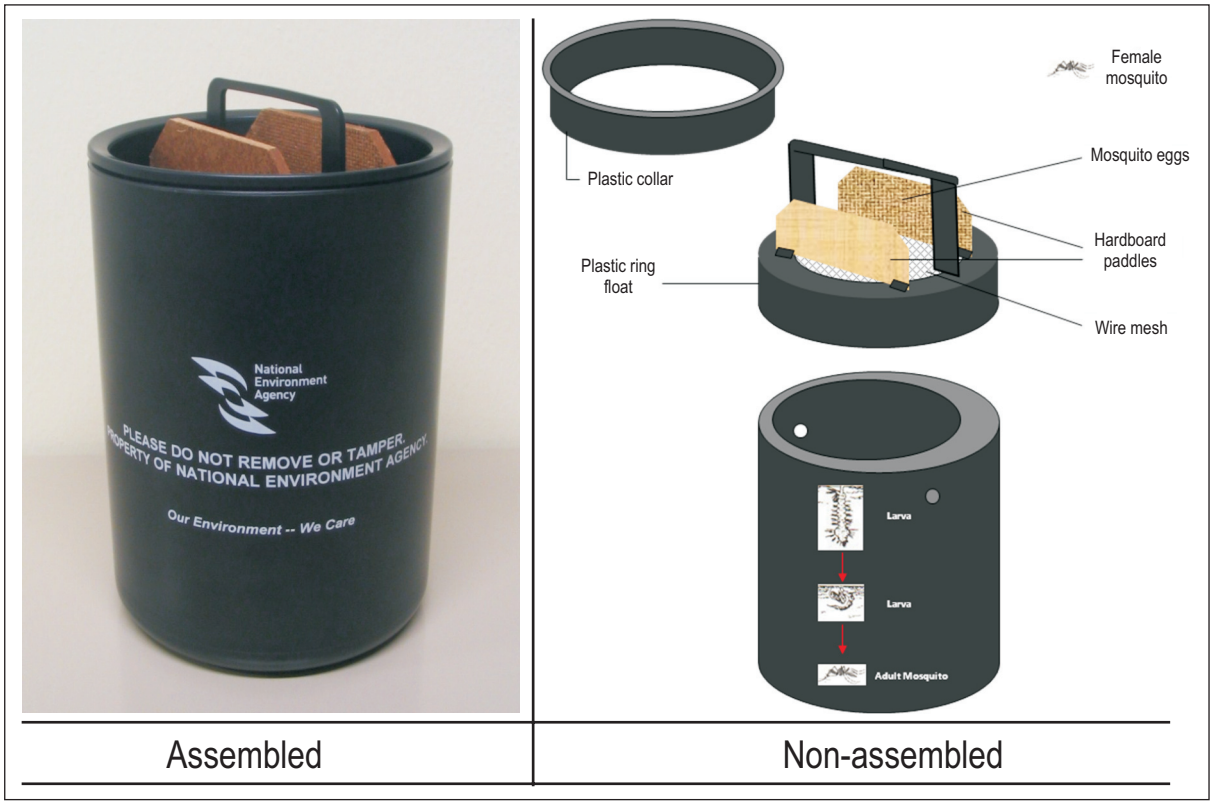
"Ovitraps" are devices used to detect the presence of *Ae. aegypti* and *Ae. albopictus* where the population density is low and larval surveys are largely unproductive (e.g. when the Breateau Index is less than 5), as well as under normal conditions. They are particularly useful for the early detection of new infestations in areas from which the mosquitoes have been previously eliminated. For this reason, they are used for surveillance at international ports of entry, particularly airports, which comply with the International Health Regulations (2005) and which should be maintained free of vector breeding.

An ovitrap enhanced with hay infusion has been shown to be a very reproducible and efficient method for *Ae. aegypti* surveillance in urban areas and has also been found to be useful to evaluate control programmes such as adulticidal space spraying on adult female populations.[88]

The standard ovitrap is a wide-mouthed, pint-sized glass jar, painted black on the outside. It is equipped with a hardboard or wooden paddle clipped vertically to the inside with its rough side facing inwards. The jar is partially filled with water and is placed appropriately in a suspected habitat, generally in or around homes. The "enhanced CDC ovitrap" has yielded eight times more *Ae. aegypti* eggs than the original version. In this method, double ovitraps are placed. One jar contains an olfactory attractant made from a "standardized" seven day-old infusion while the other contains a 10% dilution of the same infusion. Ovitraps are usually serviced on a weekly basis, but in the case of enhanced ovitraps are serviced every 24 hours. The paddles are examined under a dissecting microscope for the presence of *Ae. aegypti* eggs, which are then counted and stored.

Where both *Ae. aegypti* and *Ae. albopictus* occur, eggs should be hatched and then the larvae or adults identified, since the eggs of those species cannot be reliably distinguished from each other. The percentage of positive ovitraps provides a simple index of infestation levels. Again, if the eggs are counted it can provide an estimate of the adult female population. Figure 10 illustrates assembled and non-assembled ovitraps.

Figure 10: Ovitrap



Source: National Environment Agency, Ministry of Environment and Water Resource, Singapore, 2008.[89]

Tyre section larvitraps

Tyre section larvitraps of various designs have also been used for monitoring oviposition activity. The simplest among these is a water-filled radial section of an automobile tyre. A prerequisite for any design is that it must either facilitate visual inspection of the water *in situ* or allow the ready transfer of the contents to another container for examination. Tyre larvitraps differ from ovitraps in that water level fluctuations brought about by rainfall induce the hatching of eggs; hence the presence of larvae is noted instead of the paddles on which eggs have been deposited.[v]

Epidemiological interpretation of vector surveillance

Adult surveillance

The epidemiology of dengue infection may be complicated because *Ae. aegypti* may probe repeatedly on one or more persons during a single blood meal. The correlation of different entomological indices in terms of actual disease transmission is difficult. The interpretation of the epidemiology of dengue transmission must take into account inter-urban population movement, focality of *Aedes* populations within the urban area, and fluctuations in adult population densities, all of which influence transmission intensity. More attention should be given to understanding the relationships among adult vector densities, densities of the human population in different parts of the city, and the transmission of dengue viruses.

v The placement and use of this method is discussed in detail by Nathan M.B.. et al.[84]

Larval surveillance

The commonly-used larval indices (house, container and Breateau) are useful for determining general distribution, seasonal changes and principal larval habitats, as well as for evaluating environmental sanitation programmes. They have direct relevance to the dynamics of disease transmission. However, the threshold levels of vector infestation that constitute a trigger for dengue transmission are influenced by many factors, including mosquito longevity and immunological status of the human population. There are instances (e.g. in Singapore), where dengue transmission occurred even when the House Index was less than 2%.[90]

Therefore, the limitations of these indices must be recognized and studied more carefully to determine how they correlate with adult female population densities, and how all indices correlate with the disease-transmission risk. The development of alternative, practical and more sensitive entomological surveillance methodologies is an urgent need. The level and type of vector surveillance selected by each country or control programme should be determined by operational research activities conducted at the local level.

7.4 Sampling approaches

The sample size for routine larval surveys should be calculated using statistical methods based on the expected level of infestation and the desired level of confidence in the results. Annex 4 gives tables and examples on how to determine the number of houses to be inspected. Several approaches as in *Box 20* can be used.

Box 20: Sampling approaches

Systematic sampling:

Every nth house is examined throughout the 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 would be inspected. This is a practical option for rapid assessment of vector population levels, especially in areas where there is no house numbering system.

Simple random sampling:

The houses to be examined are obtained from a table of random numbers (obtained from statistical textbooks 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.

Stratified random sampling:

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

Frequency of sampling

The sampling frequency would depend on the objective of the control programme. It should be decided on a case-by-case basis taking into consideration the life-cycle of the mosquito.

Control programmes using integrated strategies do not require sampling at frequent intervals to assess the impact of the applied control measures. This is especially true where the effect of the alternative strategies outlasts residual insecticides (example, larvivorous fish in large potable water-storage containers, source reduction or mosquito-proofing of containers) or when larval indices are high (HI greater than 10%).

On the other hand, feedback at least on a monthly basis may be desirable to monitor and guide community activities and to identify the issues that need more scrutiny, especially when the HI is 10% or lower. For specific research studies, it may be necessary to sample on a weekly, daily or even hourly basis (e.g. to determine the diurnal pattern of biting activity).

7.5 Monitoring insecticide resistance

Information on the susceptibility of *Ae. aegypti* to insecticides is of fundamental importance for the planning and evaluation of control. The status of resistance in a population must be carefully monitored in a number of representative sentinel sites depending on the history of insecticide usage and eco-geographical situations, to ensure that timely and appropriate decisions are made on issues such as use of alternative insecticides or change of control strategies.

During the past 40 years, chemicals have been widely used to control mosquitoes and other insects from spreading diseases of public health importance. As a result, *Ae. aegypti* and other dengue vectors in several countries[91] have developed resistance to commonly-used insecticides, including DDT, temephos, malathion, fenthion, permethrin, propoxur and fenitrothion. However, the operational impact of resistance on dengue control has not been fully assessed.[w]

In countries where DDT resistance has been widespread, precipitated resistance to currently-used pyrethroid compounds that are being increasingly used for space spray is a challenge as well. Since both groups of insecticide have the same mode of action which acts on the same target site, the voltage-gated sodium channel and mutations in the *kdr* gene have been associated with resistance to DDT and pyrethroid insecticides in *Ae. aegypti*.

It is, therefore, advisable to obtain baseline data on insecticide susceptibility before insecticidal control operations are started, and to continue periodically monitoring susceptibility levels of larval or adult mosquitoes. WHO kits[x] for testing the susceptibility of adults and larval mosquitoes remain the standard methods for determining the susceptibility of *Aedes* populations.[92]

Biochemical and immunological techniques for testing individual mosquitoes have also been developed and are yet available for routine field use.

7.6 Additional information for entomological surveillance

In addition to the evaluation of aspects such as vector density and distribution, community-oriented, integrated pest management strategies require that other parameters be periodically monitored. These include the distribution and density of the human population, settlement characteristics, and conditions of land tenure, housing styles and education.

The monitoring of these parameters is relevant and of importance to planning purposes and for assessing the dengue risk. Knowledge of changes over time in the distribution of water supply

w Ranson H, Burhani J, Lumjuan N, Black WC. Insecticide resistance in dengue vectors, 2010. TropIKA.net Journal; 1(1). http://journal.tropika.net/scielo.php?script=sci_arttext&pid=S2078-86062010000100003&lng=en&nrm=iso&tlng=en

x Instructions for testing and purchase of kits, test papers and solutions are available at http://www.who.int/entity/whopes/resistance/en/WHO_CDS_CPE_PVC_2001.2.pdf

services, their quality and reliability, as well as in domestic water-storage and solid waste disposal practices is also particularly relevant. Meteorological data are important as well. Such information aids in planning targeted source reduction and management activities, as well as in organizing epidemic interventions measures.

Some of these data sets are generated by the health sector, but other sources of data may be necessary. In most cases, annual or even less frequent updates will suffice for programme management purposes. In the case of meteorological data, especially rainfall patterns, humidity and temperature, a more frequent analysis is warranted if it is to be of predictive value in determining seasonal trends in vector populations and their short-term fluctuations.

8. Dengue Vectors

8.1 Biology of *Aedes aegypti* and *Aedes albopictus*

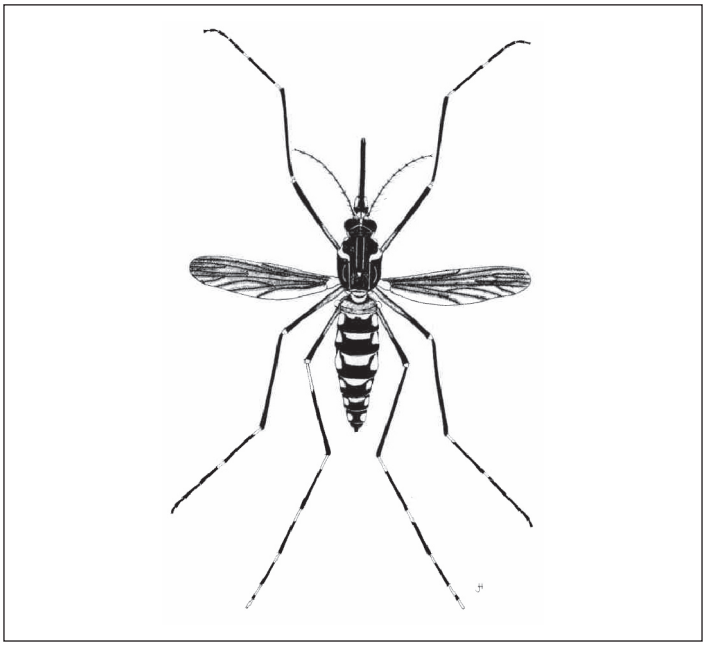
In the South-East Asia Region of WHO, *Aedes aegypti* (or *Ae. aegypti, and* also known as *Stegomyia aegypti*)[93] is the principal epidemic vector of dengue viruses. *Aedes albopictus* (*Ae. albopictus*) has been recognized as a secondary vector that is also important in the maintenance of the viruses.

Aedes aegypti

Taxonomic status

Ae. aegypti exhibits a continuous spectrum of scale patterns across its range of distribution from a very pale form to a dark form, with associated behavioural differences.[94] It is essential to understand the bionomics of the local mosquito population as a basis for its control (Figure 11).

Figure 11: *Ae. aegypti* (female)



Source: D.S. Kettle, Medical and Veterinary Entomology. 2nd Edition. CAB International. 1995. p. 110.[95]

Geographical distribution in South-East Asia

Distribution

Ae. aegypti is widespread in tropical and subtropical areas of South-East Asia. Its distribution appears to be related to the 20 °C isotherm, which roughly correlates with the tropical zone between latitude 40°N and 40°S. It is most common in urban areas. The rural spread of *Ae. aegypti* is a relatively recent occurrence associated with developmental and infrastructural growth initiatives such as expansion of rural water supply schemes and improved transport systems *(see Figure 4a)*.

In semi-arid areas as in parts of India, *Ae. aegypti* is an urban vector and populations typically fluctuate with rainfall and water storage habits.[96] In other countries of South-East Asia where the annual rainfall is generally greater than 200 cm, *Ae. aegypti* populations are more stable and established in urban, semi-urban and rural areas. Because of traditional water storage practices in Indonesia, Myanmar and Thailand, their densities are higher in semi-urban areas than in urban areas.

Urbanization tends to increase the number of habitats suitable for *Ae. aegypti*. In some cities where vegetation is abundant, both *Ae. aegypti* and *Ae. albopictus* occur together. But *Ae. aegypti* is generally the dominant species, depending on the availability and type of larval habitat and the extent of urbanization. The premise index for *Ae. aegypti* was the highest in slum houses, shop houses and multistoreyed flats. *Ae. albopictus,* on the other hand, did not seem to relate to the prevailing housing type in its distribution but tended to occur more commonly in areas with open spaces and vegetation.

Altitude

Altitude is an important factor in limiting the distribution of *Ae. aegypti*. In India, *Ae. aegypti* ranges from sea level to heights of approximately 1200 metres above sea level. Lower elevations (less than 500 metres) have moderate to heavy mosquito populations while mountainous areas (higher than 500 metres) have low populations.[97] In countries of South-East Asia, an altitude of 1000 to 1500 metres appears to be the limit for *Ae. aegypti* distribution. In other regions of the world, it is found at even higher altitudes, for example, up to 2200 metres[98] in Columbia.

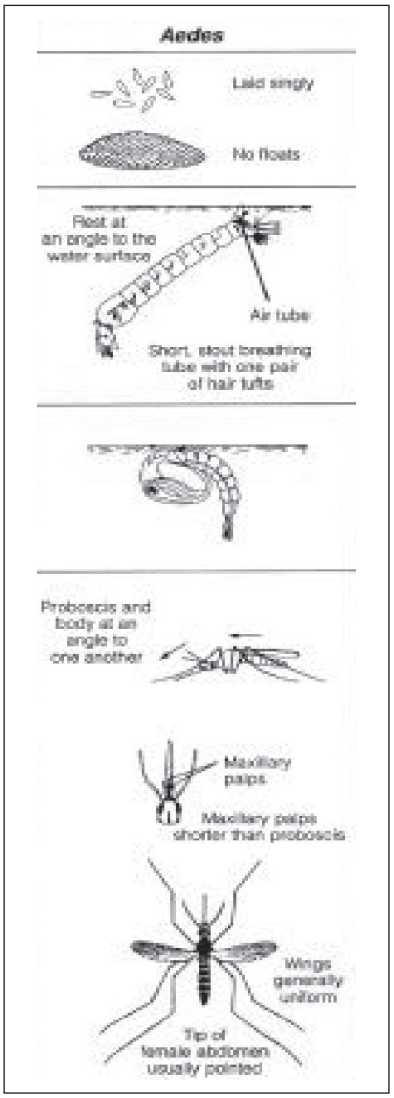
Life-cycle

The mosquito has four distinct stages in its life-cycle: egg, larva, pupa and adult *(Figure 12)*.

Eggs

The female *Ae. aegypti* lays about 50 to 120 eggs in small containers such as flower vases, water-storage jars and other indoor water recepticles, as well as in rainwater collected in small containers such as cups, tyres, etc. outdoors. Eggs are deposited

Figure 12: Life-cycle of *Ae. aegypti*



Source: *Bruce-Chwatt L.J.. Essential Malariology. 1985, John Wiley and Sons New York. http://www.ifrc.org/docs/pubs/health/chapter5a.pdf*

singly on damp surfaces just above the waterline. Most female *Ae. aegypti* lay eggs in several oviposition sites during a single gonotrophic cycle. Embryonic development is usually completed in 48 hours in a warm and humid environment. Once the embryonic development is complete, the eggs can withstand long periods of desiccation (for more than a year). Eggs hatch once the containers are flooded, but not all eggs hatch at the same time. The capacity of eggs to withstand desiccation facilitates the survival of the species in adverse climatic conditions.

Larvae and pupae

The larvae pass through four developmental stages. The duration of the larval development depends on temperature, availability of food and larval density in the receptacle. Under optimal conditions, the time taken from hatching to the emergence of the adult can be approximatey 10 days and as short as seven days, including two days in the pupal stage. At low temperatures, however, it may take several weeks for adults to emerge.

Throughout most of South-East Asia, *Ae. aegypti* oviposits almost entirely in domestic and man-made water receptacles.[y] These include a multitude of receptacles found in and around urban environments (households, construction sites and factories) such as water-storage jars, saucers on which flowerpots rest, flower vases, cement baths, foot baths, wooden and metal barrels, metal cisterns, discarded tyres, bottles, tin cans, polystyrene containers, plastic cups, discarded wet-cell batteries, glass containers associated with "spirit houses" (shrines), drainpipes and ant-traps in which the legs of cupboards and tables are often rested.

Natural larval habitats are rare, but include tree holes, leaf axils and coconut shells. In hot and dry regions, overhead tanks and groundwater-storage tanks may be primary habitats. In areas where water supplies are irregular, inhabitants store water for household use, thereby increasing the number of available larval habitats.

While such man-made water receptacles may be removed to deny the *Ae. aegypti* a breeding habitat, one must also be prepared to eliminate other unconventional breeding habitats that the mosquito would be forced to find.

Adults

Soon after emergence, the adult mosquitoes mate and the inseminated female may take a blood meal within 24–36 hours. Blood is the source of protein essential for the maturation of eggs. *Ae. aegypti*, being a discordant species, takes more than one blood meal to complete one gonotropic cycle. This behaviour increases man–mosquito contact and is of great epidemiological importance.

Feeding behaviour

Ae. aegypti is highly anthropophilic, although it may feed on other available warm-blooded animals. Being a diurnal species, females have two periods of biting activity: one in the morning for several hours after daybreak and the other in the afternoon for several hours before dark.[99,100,101] The actual peaks of biting activity may vary with location and season.

Ae. aegypti, being a nervous feeder, may feed on more than one person. This behaviour greatly increases its epidemic transmission efficiency. Thus, it is not uncommon to see several members of the same household with an onset of illness occurring within 24 hours, suggesting that they were infected by the same infective mosquito.[19] *Ae. aegypti* generally does not bite at night, but it will feed at night in lighted rooms.[100]

y Visual representations of potential breeding habitats are available at http://www.dengue.gov.sg/ subject.asp?id=155

Resting behaviour

More than 90% of the *Ae. aegypti* population rests on non-sprayable surfaces, namely dark, humid, secluded places inside houses or buildings, including bedrooms, closets, bathrooms and kitchens. Less often is it found outdoors in vegetation or other protected sites. The preferred indoor resting surfaces are the undersides of furniture, hanging objects such as clothes and curtains, and walls. Hence, indoor residual spray is not an option for its control as with malaria vectors.

Flight range

The dispersal of adult female *Ae. aegypti* is influenced by a number of factors including the availability of oviposition sites and blood meals, but appears to be often limited to within 30–50 metres of the site of emergence. However, recent studies in Puerto Rico (USA) indicate that they may disperse more than 400 metres primarily in search of oviposition sites.[102] Passive transportation can occur via desiccated eggs and larvae in containers.

Longevity

The adult *Ae. aegypti* has a lifespan of about 3–4 weeks. During the rainy season, when survival is longer, the risk of virus transmission is greater. More research is required on the natural survival of *Ae. aegypti* under various environmental conditions.

Virus transmission

A vector mosquito may become infected when it feeds on a viraemic human host. In the case of DF/DHF, viraemia in the human host may occur 1–2 days before the onset of fever and lasts for about five days after the onset of fever.[103] After an intrinsic incubation period of 10–12 days, the virus grows through the midgut to infect other tissues in the mosquito, including the salivary glands. If it bites other susceptible persons after the salivary glands become infected, it transmits dengue virus to those persons by injecting the salivary fluid.

Aedes albopictus

Ae. albopictus (*Figure 13*) belongs to the same subgenus (*Stegomyia*) as *Ae. aegypti*. This species is widely distributed in Asia in both tropical and temperate countries. During the past two decades, the species has extended its range (*Figure 4b*) to North and South America including the Caribbean, Africa, Southern Europe and some Pacific islands.[104] It is estimated that the northern limit for over-wintering *Ae. albopictus* is the 0 ^{0}C isotherm, and in summer its northward expansion is –5 ^{0}C isotherm, much further north than *Ae. aegypti* can colonize.[95]

Figure 13: *Aedes albopictus*

Source: *http://www.invasive.org/browse/detail.cfm?imgnum=1366025*

Ae. albopictus is primarily a forest species that has adapted to rural, suburban and urban human environments. It oviposits and develops in tree holes, bamboo stumps and leaf axils in forest habitats; and in artificial containers in urban settings. It is an indiscriminate blood feeder and more zoophagic than Ae. *aegypti*. Its flight range may be up to 500 metres.

Unlike *Ae. aegypti*, some strains in northern Asia and America are adapted to the cold, with eggs that can spend the winter in diapause. In some areas of Asia and the Seychelles, *Ae. albopictus* has been occasionally incriminated as the vector of epidemic DF/DHF though it is much less important than *Ae. aegypti*. In the laboratory, both species can transmit dengue virus vertically from a female through the eggs to her progeny, although *Ae. albopictus* does so more readily.[105]

Taxonomic status

Ae. alobopictus can be easily recognized from other stegomyia species by the following combination of characters: palpi with white scales, scutum with a long, medium longitudinal white stripe extending from the interior margin to about the level of wing root *(Figure 13)*.

Geographical distribution in South-East Asia

Ae. alobopictus is widespread in all countries of South-East Asia. It is believed that the species originated from this region of the world.[106]

Altitude

Basically *Ae. albopictus* is a feral species most commonly found in fringe areas of forests. The presence of this species deep inside the forest is questionable. In Thailand, *Ae. albopictus* has been collected in three forested habitats in elevations ranging from 430 metres to 1800 metres.[107]

Life-cycle

The species has four distinct stages in its life-cycle: egg, larva, pupa and adult.[106]

Eggs

The female mosquito lays about 100 eggs that can withstand desiccation for long periods. Eggs hatch on flooding.

Larve and pupae

Under laboratory conditions, the larval stages at 25 °C and with optional food take 5 to 10 days to transform to the pupal stage, which takes two more days to emerge as an adult. At low temperatures, the development period get prolonged. Development, however, ceases at temperatures of 11 °C and below. Being feral species the mosquito breeds in tree holes, bamboo stumps and coconut shells at forest fringes, although it invades peripheral areas of urban cities through man-made containers filled with rainwater. In parks and gardens in cities, the species breeds on flower beds and various other natural/man-made containers. While such man-made water receptacles may be removed to deny the *Ae. aegypti* a breeding habitat, one must be prepared to watch out for other more unconventional breeding habitats that the mosquito would be forced to find.

Adults

After emergence, mating occurs between adult mosquitoes and the inseminated females may take a blood meal within 24–36 hours. *Ae. albopictus* is an aggressive feeder and takes the full blood meal in one go to complete genesis, as it is a concordant species. This behaviour as well as feeding

on other mammals/birds reduces its vectorial capacity. Unlike *Ae. aegypti*, some strains are adapted to the cold of northern Asia with their eggs spending the winter in diapause.

Ae. albopictus is an efficient bridge vector between enzootic and human cycles among the human population living near the forest fringes. It is also more efficient then *Ae. aegypti* in maintaining the virus transovarially (vertically) as a reservoir.

Resting behaviour

Ae. albopictus generally rests outdoors near the ground and in any part of a forest.

Survival

Results of laboratory research with *Ae. albopictus* at 25 °C and relative humidity of 30% brought out that: i) females live longer than males; and ii) females usually live from four to eight weeks in the laboratory but may survive up to three to six months.

Vector identification

Pictorial keys to *Aedes (Stegomyia)* mosquitoes breeding in domestic containers are given in Annex 5. The keys include *Culex quinquefasciatus*, which may be found in the same habitats.[108]

9. Vector Management and Control

Dengue fever/DHF control is primarily dependent on the control of *Ae. aegypti*, since no vaccine is yet available for the prevention of dengue infection and there are no specific drugs for its treatment. Dengue vector control programmes in the South-East Asia Region have, in general, recorded modest success. Earlier attempts relied almost exclusively on space spraying of insecticides for adult mosquito control. However, space spraying required specific operations that were often not adhered to, and most countries found its costs prohibitive as well. Subsequently, source reduction by clean-up campaigns and/or larviciding with insecticides has been promoted widely. However, their success has been limited on account of the variable degrees of compliance by communities and the non-acceptability of larvicidal treatment either due to the bad odour of the larvicide used or inherent misgivings about it that are prevalent in some communities.

To achieve sustainability of a successful DF/DHF vector control programme it is essential to focus on the larval source reduction while closely cooperating with non-health sectors—such as nongovernmental organizations, civic organizations and community groups—to ensure community understanding and involvement in implementation. There is, therefore, a need to adopt an integrated approach to mosquito control by including all appropriate methods (environmental, biological and chemical) that are safe, cost-effective and environmentally acceptable. A successful and sustainable *Ae. aegypti* control programme must involve partnerships between government agencies and the community. The approaches described below are considered necessary to achieve long-term and sustainable control of *Ae. aegypti*.

9.1 Environmental management

Environmental management involves planning, organization, execution and monitoring of activities for the modification and/or manipulation of environmental factors or their interplay with human beings with a view to prevent or minimize vector breeding and reduce human-vector-virus contact. The control of *Ae. aegypti* in Cuba and Panama in the early part of the 20th century was based mainly on environmental management.[15,109] Such measures remain applicable wherever dengue is endemic. In 1982 the World Health Organization[110] defined three kinds of environmental management *(see Box 21)*.

Environmental methods to control *Ae. aegypti* and *Ae. albopictus* and reduce man-vector contact include source reduction, solid waste management, modification of man-made breeding sites, and improved house design. The major environmental management methods used for controlling immature stages of vectors are summarized in *Box 22*.

Box 21: Environmental management methods

- Environmental modification: This includes any long-lasting physical transformation of land, water and vegetation aimed at reducing vector habitats without causing unduly adverse effects on the quality of the human environment.
- Environmental manipulation: This incorporates planned recurrent activities aimed at producing temporary changes in vector habitats that involve the management of "essential" and "non-essential" containers, and the management or removal of "natural" breeding sites.
- Changes to human habitation or behaviour: These feature the efforts made to reduce man-vector-virus contact.

Box 22: Environmental measures for control of some *Ae. aegypti* production sites

Production site	Empty, clean, scrubbed weekly	Mosquito-proof cover	Store under roof	Modify design	Fill (sand/ soil)	Collect, recycle/ dispose	Puncture or drain
Essential							
Water evaporation cooler	+						
Water storage tank/ cistern	+	+		+	+		
Drum (40–55 gallons)	+	+		+			
Flower vase with water	+						
Potted plants with saucers	+						
Ornamental pool/ fountain	+						
Roof gutter/sun shades	+						
Animal water container	+						
Ant-trap	+						
Non-essential							
Used tyres		+	+		+	+	
Discarded large appliances						+	+
Discarded buckets						+	
Discarded food and drink containers						+	
Natural							
Tree holes					+		
Rock holes					+		

Environmental modification

Improved water supply

Whenever piped water supply is inadequate and available only at restricted hours or at low pressure, the storage of water in varied types of containers becomes a necessary practice that leads to increased *Aedes* breeding. The majority of such containers are often large and heavy (e.g. storage jars) and can neither be easily disposed of nor cleaned. In rural areas, unpolluted, disused wells become breeding grounds for *Ae. aegypti*. It is essential that potable water supplies be delivered in sufficient quantity, quality and consistency to reduce the necessity and use of water-storage containers that serve as the most productive larval habitats.

Mosquito-proofing of overhead tanks/cisterns or underground reservoirs

Where *Ae. aegypti* larval habitats include overhead tanks/cisterns and masonry chambers of piped waterlines, these structures should be mosquito-proofed.[111] A suggested design is illustrated in Annex 6a. Similarly, mosquito-proofing of domestic wells and underground water-storage tanks should be ensured.

Filling, land levelling and transformation of impoundment margins

These are usually of permanent nature; however, correct operation and adequate maintenance are essential for their effective functioning.

Environmental manipulation

Draining water supply installations

Water collection/leakages in masonry chambers, distribution pipes, valves, sluice valves, surface boxes for fire hydrants, water meters, etc. that serve as important *Ae. aegypti* larval habitats in the absence of preventive maintenance should be provided with soak pits (Annex 6b).

Covering domestic water-storage containers

The major sources of *Ae. aegypti* breeding in most urban areas of South-East Asia are containers storing water for household use, including clay, ceramic and cement water jars, metal drums, and smaller containers storing fresh water or rainwater. Water storage containers should be covered with tightly fitting lids or screens and care should be taken to replace them after water is used. An example of the efficacy of this approach has recently been demonstrated in Thailand.[112]

Cleaning flowerpots/vases and ant-traps

Flowerpots, flower vases and ant-traps are common sources of *Ae. aegypti* breeding. Water that collects on the saucers that are placed below flowerpots should be removed every week. Water in flower vases should be removed and discarded weekly and vases scrubbed and cleaned before reuse. Alternatively, live flowers can be placed in a mixture of sand and water. Brass flowerpots, which make poor larval habitats, can be used in cemeteries in place of traditional glass containers. Ant-traps to protect food-storage cabinets should be cleaned on a weekly basis and treated with common salt or oil.

Cleaning incidental water collections

Desert (evaporation) water-coolers, condensation collection pans under refrigerators, and air-conditioners should be regularly inspected, drained and cleaned. Desert water-coolers generally employed in arid/semi-arid regions[113] of South-East Asia to cool houses during summer contain two manufacturing defects. These are as follows:

- The exit pipe at the bottom of the water-holding tray is generally fixed a few centimetres above the bottom. This exit pipe should be fitted at such a level that while emptying the tray, all the water should get drained off without any retention at the bottom.
- Desert coolers are normally fitted to windows with the exit pipe located on the exterior portion of the tray. These sites are usually difficult to access, and therefore, there is a need to change the design so that both the filling and emptying of the water-holding trays can be manipulated from the room, thus eliminating the need for climbing to approach the exit pipe from the exterior of the building.

Each country should develop regulatory mechanisms to ensure the application of the design specifications as outlined above for manufacturing desert coolers.

Managing construction sites and building exteriors

Water-storage facilities at construction sites should be mosquito-proof. Housekeeping should also be stepped up to prevent occurrence of water stagnation. The design of buildings is important to prevent *Aedes* breeding. Drainage pipes of rooftops, sunshades/porticos often get blocked and become breeding sites for *Aedes* mosquitoes. Roof gutters of industrial/housing sheds also get similarly blocked. Where possible, the design of such features should minimize the tendency for mosquito breeding. There is a need for periodic inspection of such structures during the rainy season to locate potential breeding sites.

Managing mandatory water storage for fire-fighting

Fire prevention regulations may require mandatory water storage in some countries.[114] Such storage tanks need to be kept mosquito-proof. These drums should be kept covered with tight lids; failing which larvivorous fish or temephos sand granules (one part per million) can be used.

Managing discarded receptacles

Discarded receptacles – namely tins, bottles, buckets or any other consumable packaged items such as plastic cups/trays and waste material, etc. scattered around houses – should be removed and buried in landfills. Scrap material in factories and warehouses should be stored appropriately until disposal. Household and garden utensils (buckets, bowls and watering devices) should be kept upside down to prevent accumulation of rain water. Similarly, in coastal areas canoes and small boats should be emptied of water and turned upside down when not in use. Plant waste (coconut shells, cocoa husks, etc.) should be disposed of properly.

Managing glass bottles and cans

Glass bottles, cans and other small containers should be reused, recycled or buried in landfills.

Tyre management

Used automobile tyres are of significant importance as breeding sites for urban *Aedes*, and are therefore a public health problem. Imported used tyres are believed to be responsible for the introduction of *Ae. albopictus* into the United States of America, Europe and Africa.[115] Tyres in depots should always be kept under cover to prevent collection of rainwater. New technologies for

tyre recycling and disposal are continually coming into use, but most of them have proved to be of limited application or cost-intensive.

It is recommended that each community should look at ways to recycle/reuse used tyres so that they do not become breeding habitats. Some examples of how used tyres can be reused are mentioned below:

- As soil erosion barriers, e.g. creation of artificial reefs in order to reduce beach erosion by wave action.
- As planters or traffic/crash barriers, after filling with earth or concrete.
- As sandals, floor mats, industrial washers, gaskets, buckets, garbage pails and carpet backing, etc. (after recycling).
- As durable, low-cost refuse containers by using larger tyres such as truck tyres.

Filling up of cavities of fences

Fences and fence-posts made from hollow trees such as bamboo should be cut down to the node, and concrete blocks should be filled with packed sand or cement to eliminate potential *Aedes* larval habitats.

Managing public places

Municipalities should have in place a programme to inspect and maintain structures in public places such as street lamp posts, park benches and litter bins that may collect water if not regularly checked. Discarded receptacles that may hold water such as plastic cups, broken bottles and metal cans should be regularly removed from public areas.

Personal protection

Protective clothing

Clothing reduces the risk of mosquito bite if the cloth material is sufficiently thick or loosely fitting. Long sleeves and trousers with stockings may protect the arms and legs, which are the preferred sites for mosquito bites. Schoolchildren should adhere to these practices whenever possible.

Mats, coils and aerosols

Household insecticidal products, namely mosquito coils and aerosols, are used extensively for personal protection against mosquitoes. Electric vaporizer mats and liquid vaporizers are more recent additions, and are marketed in practically all urban areas.

Repellents

Repellents are common means of personal protection against mosquitoes and other biting insects. These are broadly classified into two categories, natural repellents and chemical repellents.

Essential oils from plant extracts are the main natural repellent ingredients, such as citronella oil, lemon grass oil and *neem* oil.

Chemical repellents such as DEET (N, N-Diethyl-m-Toluamide) can provide protection against *Ae. aegypti, Ae. albopictus* and anopheline species for several hours. A new compound, picaridin [2-(2-hydroxyethyl)-1-piperidinecarboxylic acid 1-methylpropyl ester] is very effective against mosquitoes. It has low toxicity and efficacy levels comparable with that of DEET.[116] Permethrin is an effective repellant when impregnated in cloth. Table 11 presents the names of the principal insect repellents and the duration of protection.

Table 11: Insect repellents and length of duration

Main ingredient	Duration	Formulation
DEET[z] <10%	1–3 h	Pump spray, aerosol, gel, lotion.
DEET 10%–30%	4–6 h	Pump spray, aerosol, lotion, stick.
DEET 20%–33%, extended duration	6–12 h	Lotion, aerosol.
Citronella oil 5%–15%	20–30 min	Pump spray, lotion, oil, towelette.
Lemon eucalyptus oil 10%–30%	2–5 h	Lotion.
Picaridin 7%	3–4 h	Pump spray.
Picaridin 15%	6–8 h	Aerosol.
Permethrin[aa] 0.5%+	Several washings	Aerosol, pump spray.

Source: Katz T.M., Miller J.H., Hebert A.A.. Insect repellents: Historical perspectives and new developments. J Am Acad Dermatol. 2008 May; 58(5): 865–71.[116]

Insecticide-treated materials: Mosquito nets and curtains

Insecticide-treated mosquito nets (ITNs)[117,118] have limited utility in dengue control programmes since the vector species bites during the day. However, treated nets can be effectively utilized to protect infants and night workers who sleep by day. They can also be effective for people who generally have an afternoon nap. Details of insecticide treatment of mosquito nets and curtains are explained in Annex 7.

The long-lasting insecticidal net (LLIN) is a factory-treated mosquito net with insecticide (synthetic pyrethroids) either incorporated into or coated around the fibre. It is expected to retain its biological activity for a minimum number of WHO washes and a minimum period of time under field conditions. Currently, an LLIN is expected to retain its biological activity for at least 20 standard WHO washes under laboratory conditions and three years of recommended use under field conditions.[119]

9.2 Biological control

Biological control is based on the introduction of organisms that prey upon, parasitize, compete with or otherwise reduce populations of the target species.[66] The application of biological control agents, which are directed against the larval stages of dengue vectors, in South-East Asia has been somewhat restricted to specific container habitats in small-scale field operations. While biological control avoids chemical contamination of the environment, there may be operational limitations such as the expense and task of rearing the organisms on a large scale, difficulty in applying them and their limited utility in aquatic sites where temperature, pH and organic pollution may exceed the narrow requirements of the organism. Importantly, the biological control organisms are not resistant to desiccation, hence their utility is mainly restricted to container habitats that are seldom emptied or cleaned, such as large water-storage containers or wells. However, the willingness of communities to accept the introduction of organisms into water containers is essential. Community involvement is also desirable in distributing the agents, and monitoring and restocking containers, as necessary.

z DEET, N,N-diethyl-3-methylbenzamide.
aa Permethrin is not formulated for direct application to the skin.

Fish

Larvivorus fish (*Gambusia affinis* and *Poecilia reticulata*) have been extensively used for the control of *An. stephensi* and/or *Ae. aegypti* in large waterbodies or large water containers in many countries in South-East Asia (for example, the community-based use of larvivorous fish *Poecilia reticulata* to control the dengue vector *Ae. aegypti* in domestic water-storage containers in rural Cambodia).[120] The applicability and efficiency of this control measure depends on the type of containers used.

Bacteria

Two species of endotoxin-producing bacteria, *Bacillus thuringiensis* serotype H-14 *(Bt.H-14)* and *Bacillus sphaericus (Bs),* are effective mosquito control agents. They do not affect non-target organisms associated with mosquito larvae. *Bt.H-14* has an extremely low-level mammalian toxicity and has been accepted for the control of mosquitoes in containers storing water for household use.[121] *Bt.H-14* has been found to be most effective against *An. stephensi* and *Ae. aegypti*, while *Bs* is the most effective against *Culex quinquefasciatus* which breeds in polluted water.

There is a whole range of formulated *Bti* products produced by several major companies for the control of vector mosquitoes. Such products include wettable powders and various slow-release formulations including briquettes, tablets and pellets. Further developments are expected in slow-release formulations. *Bt.H-14* has an extremely low-level mammalian toxicity and has been accepted for the control of mosquitoes in containers storing water for household use.

Cyclopods

The predatory role of copepod crustaceans[ab] was documented between 1930 and 1950. However, scientific evaluation was carried out only in 1980 in Tahiti, French Polynesia, where it was found that *Mesocyclops aspericornis* could effect a 99.3% mortality rate among *Aedes (Stegomyia)* larvae and 9.7% and 1.9%, respectively among *Cx. quinquefasciatus* and *Toxorhynchities amboinensis* larvae.[122] Trials in crab burrows against *Ae. polynesiensis* and in water tanks, drums and covered wells met with mixed results.

In Queensland, Australia, of seven species evaluated in the laboratory all but *M. notius* were found to be effective predators of both *Ae. aegypti* and *An. farauti* but not against *Cx. quinquifasciatus*. Field releases in both northern and southern Queensland, however, showed mixed results. In Thailand too, the results were mixed; but in Vietnam the results were more successful, contributing to the eradication of *Ae. aegypti* from one village.[123]

Although the lack of nutrients and frequent cleaning of some containers can prevent the sustainability of copepods, they could be suitable for large containers that cannot be cleaned regularly (wells, concrete tanks and tyres).[123] They can also be used in conjunction with *Bt.H-14*. Copepods have a role in dengue vector control, but more research is required on the feasibility of operational use.

Autocidal ovitraps

Autocidal ovitraps were successfully used in Singapore as a control device in the eradication of *Ae. aegypti* from the Paya Lebar International Airport.[124] In Thailand, the autocidal trap was further modified as an auto-larval trap using plastic material available locally. Unfortunately, under local conditions of water-storage practices in Thailand, the technique was not very efficient in reducing

ab Copepods should not be used in countries where Gnathostomiasis are endemic as they may act as intermediate hosts for these parasites.

natural populations of *Ae. aegypti*. Better results can be expected if the number of existing potential larval habitats is reduced, or more autocidal traps are placed in the area under control, or both activities are carried out simultaneously. It is believed that under certain conditions this technique could be an economical and rapid means of reducing the natural density of adult females as well as serve as a device for monitoring infestations in areas where some reduction in the population density of the vector has already taken place. However, successful application of autocidal ovitraps/larval traps depends on the number placed, the location of placement, and their attractiveness as *Ae. aegypti* female oviposition sites.[125]

9.3 Chemical control

Chemicals have been used to control *Ae. aegypti* since the beginning of the 20th century. In the first campaigns against the yellow fever vector in Cuba and Panama, along with widespread clean-up campaigns, *Aedes* larval habitats were treated with oil and homes were fumigated with pyrethrins. When the insecticidal properties of DDT were discovered in the 1940s, this compound became a principal method of *Ae. aegypti* eradication programmes in the Americas. When resistance to DDT emerged in the early 1960s, organophosphate insecticides, including fenthion, malathion and fenitrothion, were used for *Ae. aegypti* adult control and temephos as a larvicide. Current methods of applying insecticides include larvicide application and space spraying.[125]

Chemical larviciding

Larviciding or "focal" control of *Ae. aegypti* is usually limited to domestic-use containers that cannot be destroyed, eliminated or otherwise managed. It is difficult and expensive to apply chemical larvicides on a long-term basis. Therefore, chemical larvicides are best used in situations where the disease and vector surveillance indicate the existence of certain periods of high risk and in localities where outbreaks might occur.

Establishing the precise timing and location are essential to ensure maximum effectiveness. Control personnel distributing the larvicide should always encourage house occupants to control larvae by environmental sanitation, i.e source reduction. There are three insecticides that can be used for treating containers that hold drinking water.[ac] The WHO guidelines on drinking water quality[126] provide guidance on the use of pesticides in drinking water.

Temephos 1% sand granules

One per cent temephos sand granules are applied to 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, especially in porous earthen jars under normal water use patterns. The quantity of sand granules required to treat various sizes of water containers is presented in Annex 8. The susceptibility level of *Aedes* mosquitoes should be monitored regularly in order to ensure effective use of the insecticide.

Insect growth regulators (IGR)/pyriproxyfen

Insect growth regulators (IGRs) interfere with the development of the immature stages of the mosquito by interference of chitin synthesis during the moulting process in larvae or by disruption of the pupal and adult transformation processes.

Pyriproxyfen is an insect-juvenile hormone analogue that has been found extremely effective against *Ae. aegypti* at concentrations as low as 1 ppb or less, while high concentration does not inhibit oviposition.[127] Very low doses of pyriproxyfen can also sub-lethally affect adults by decreasing

ac *http://www.who.int/water_sanitation_health/dwq/gdwq3rev/en/*

fecundity or fertility and the contaminated adult female can transfer effective doses to any breeding sites subsequently visited by the female.[128] New formulations of pyriproxyfen[129] can retain efficacy for six months. However, the disadvantages include non-visibility since the mode of action prevents eclosion and larvae and pupae remain visibly active after treatment. As a result, suspicion among communities about the IGR's effectiveness regarding treatment of domestic water is yet another impediment.

Bacillus thuringiensis H-14 (Bt.H-14)

Bt.H-14, which is commercially available under a number of trade names, is a proven and environmentally non-intrusive mosquito larvicide. It is entirely safe for humans when the larvicide is used in drinking water in normal dosages.[121] Slow-release formulations of *Bt.H-14* have been developed. Briquette formulations that appear to have greater residual activity are commercially available and can be used with confidence in drinking water.

The use of *Bt.H-14* is described in the section on biological control. The large parabasal body that forms in this agent contains a toxin that degranulates solely in the alkaline environment of the mosquito midgut. The advantage of *Bt.H-14* is that an application destroys larval mosquitoes but spares any entomophagus predators and other non-target species that may be present. *Bt.H-14* formulations tend to rapidly settle at the bottom of water containers, and frequent applications are therefore required. The toxin is also photolabile and is destroyed by sunlight.

Space sprays

Space spraying involves the application of small droplets of insecticide into the air in an attempt to kill adult mosquitoes. It has been the principal method of DF/DHF control used by most countries in the South-East Asia Region for 25 years. Unfortunately, it has not been effective, as illustrated by the dramatic increase in DHF incidence in these countries during the same period.

Recent studies have demonstrated that the method has little effect on the mosquito population, and thus on dengue transmission.[130,131,132] Moreover, when space spraying is conducted in a community, it creates a false sense of security among residents, which has a detrimental effect on community-based source reduction programmes. From a political viewpoint, however, it is a desirable approach because it is highly visible and conveys the message that the government is taking action. This, however, is a poor justification for using space sprays**.**

Space spraying of insecticides (fogging) should not be used except in an epidemic situation. However, the operations should be carried out at the right time, at the right place, and according to the prescribed instructions with maximum coverage; so that the fog penetration effect is complete enough to achieve the desired results.

When space sprays are employed, it is important to follow the instructions on both the application equipment and the insecticide label and to make sure that the application equipment is well maintained and properly calibrated. Droplets that are too small tend to drift beyond the target area while large droplets fall out rapidly. Nozzles for ultra-low volume ground equipment should be capable of producing droplets in the 5–27 micron range and the mass median diameter should not exceed the droplet size recommended by the manufacturer.

Desirable spray characteristics include a sufficient period of suspension in the air with suitable drift and penetration into target areas with the ultimate aim of impacting adult mosquitoes. Generally, there are two forms of space spray that have been used for *Ae. aegypti* control, namely "thermal fogs" and "cold fogs". Both can be dispensed by vehicle-mounted or hand-operated machines.

Thermal fogs

Thermal fogs containing insecticides are normally produced when a suitable formulation condenses after being vaporized at a high temperature. Generally, a thermal fogging machine employs the resonant pulse principle to generate hot gas (over 200 °C) at high velocity. These gases atomize the insecticide formulation instantly so that it is vaporized and condensed rapidly with only negligible formulation breakdown. Thermal fogging formulations can be oil-based or water-based. The oil-based (diesel or kerosene) formulations produce dense clouds of white smoke, whereas water-based formulations produce a colourless fine mist. The droplet (particle) size of a thermal fog is usually less than 15 microns in diameter. The exact droplet size depends on the type of machine and operational conditions. However, uniform droplet size is difficult to achieve in normal fogging operations.

Ultra-low volume (ULV), aerosols (cold fogs) and mists

Ultra-low volume (ULV) involves the application of a small quantity of concentrated liquid insecticides. The use of less than 4.6 litres/ha of an insecticide concentrate is usually considered as an ULV application. ULV is directly related to the application volume and not to the droplet size. Nevertheless, droplet size is important and the equipment used should be capable of producing droplets in the 10–15 micron range, although the effectiveness changes little when the droplet size range is extended to 5–25 microns. The droplet size should be monitored by exposure on Teflon or silicone-coated slides and examined under a microscope. Aerosols, mists and fogs may be applied by portable machines, vehicle-mounted generators or aircraft equipment.

- **House-to-house application using portable equipment:** Portable spray units can be used when the area to be treated is not very large or in areas where vehicle-mounted equipment cannot be used effectively. This equipment is meant for restricted outdoor use and for enclosed spaces (buildings) of not less than 14 m^3. Portable application can be made in congested low-income housing areas, multi-storeyed buildings, warehouses, covered drains, sewage tanks and residential or commercial premises. 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 adequately and hence two or three operators are required per machine.
- **Vehicle-mounted fogging:** Vehicle-mounted aerosol generators can be used in urban or suburban areas with a good road system. One machine can cover up to 1500–2000 houses (or approximately 80 ha) per day. It is necessary to calibrate the equipment, vehicle speed and swath width (60–90 m) to determine the coverage obtained by a single pass. A good map of the area showing all roads is of great help in undertaking the application.

  Advocacy and communication efforts may be required to persuade residents to cooperate by opening their doors and windows. The speed of the vehicle and the time of day of application are important factors to consider when insecticides are applied by ground vehicles. The vehicle should not travel faster than 16 kilometres per hour (kph) [10 miles per hour (mph)]. The insecticide should not be applied when the wind speed is greater than 16 kph or when the ambient air temperature is greater than 28 °C (82 °F).[133,134] The best time for application is in the early morning (approximately 0600–0830 hours) or late afternoon (1700–1930 hours). Details of procedures, timing, frequency of thermal fogging and ULV space operation are given in Annex 9.

Performance of fogging machines

Estimates have been made of the average coverage per day with certain aerosol and thermal fog procedures (*Box 23*).

Box 23: Average coverage per day with space spraying procedures

Equipment	Possible daily coverage
1. Vehicle-mounted cold fogger	225 ha
2. Vehicle-mounted thermal fogger	150 ha
3. Back-pack ULV mist blower	30 ha
4. Hand-carried thermal fogger swing fog	5 ha
5. Hand-carried ULV aerosol generators	5 ha or 250 houses

Insecticide formulations for space sprays

Organophosphate insecticides such as malathion, fenitrothion and pirimiphos methyl have been used for the control of adult *Aedes* vectors. Undiluted technical grade malathion (active ingredient 95%+) or one part technical grade diluted with 24 parts of diesel have been used for ULV spraying and thermal fogging respectively. For undiluted technical grade ULV malathion applications from vehicles, the dosage on an area basis is 0.5 litres per hectare.

Apart from the above-mentioned formulations, a number of companies produce pyrethroid formulations containing either permethrin, deltamethrin, lambda-cyhalothrin or other compounds which can be used for space spray applications. It is important not to under-dose during operational conditions. Low dosages of pyrethroid insecticides are usually more effective indoors than outdoors. Also, low dosages are usually more effective when applied with portable equipment (close to or inside houses) than with vehicle-mounted equipment, even if wind and climatic conditions are favourable for outdoor applications.

Outdoor permethrin applications without a synergist should be applied at concentrations ranging from 0.5% to 1.0%, particularly in countries with limited resources and a paucity of staff experienced in routine spraying operations. Regardless of the type of equipment and spray formulations and concentrations used, an evaluation should be made from time to time to check if effective vector control is being achieved.

Insecticides suitable as cold aerosols and for thermal fogging for mosquito control are described in *Table 12*.

Safety precautions for chemical control

All pesticides are toxic to some degree. Safety precautions should therefore be followed. These include care in handling of pesticides, safe work practices for those who apply them, and their appropriate use in and around occupied housing. A safety measure for insecticide application is described in Annex 10.

Table 12: Some insecticides suitable for cold aerosol or thermal fog applications against mosquitoes

Insecticide	Chemical	Dosage of a.i[ad] (g/ha)		WHO hazard classification of Ai
		Cold aerosols	Thermal fogs[ae]	
Fenitrothion	Organophosphate	250–300	250–300	II
Malathion	Organophosphate	112–600	500–600	III
Pirimiphos-methyl	Organophosphate	230–330	180–200	III
Bioresmethrin	Pyrethroid	5	10	U
Cyfluthrin	Pyrethroid	1–2	1–2	II
Cypermethrin	Pyrethroid	1–3	–	II
Cyphenothrin	Pyrethroid	2–5	5–10	II
d,d-*trans*-Cyphenothrin	Pyrethroid	1–2	2.5–5	NA
Deltamethrin	Pyrethroid	0.5–1.0	0.5–1.0	II
D-Phenothrin	Pyrethroid	5–20	–	U
Etofenprox	Pyrethroid	10–20	10–20	U
λ-Cyhalothrin	Pyrethroid	1.0	1.0	II
Permethrin	Pyrethroid	5	10	II
Resmethrin	Pyrethroid	2–4	4	III

Source: WHO 2006/2. Pesticides and their application for the control of vectors and pests of public health importance. WHO/CDS/WHOPES/GCDPP/2006.1. http://whqlibdoc.who.int/hq/2006/WHO_CDS_NTD_WHOPES_GCDPP_2006.1_eng.pdf

Monitoring and evaluation of space spray

Monitoring and evaluation of space spray is extremely important. An example of M&E of space spray and secondary transmission of DF/DHF in an urban area in Thailand is presented in *Box 24*.

Integrated control approach

Human society is divided along socioeconomic, cultural and religious lines and different types of domestic water storage practices are evident. Many such practices promote the breeding of *Ae. aegypti* and *Ae. albopictus*. This diversity is further multiplied at workplaces, i.e. offices, commercial houses/markets, industrial houses, water-based manufacturing units, etc. In view of this diversity, the intervention tools described earlier should be evidence-based and all control measures should be suitably integrated with each specific and particular situation or case.

ad a.i—Active ingredient; Class II, moderately hazardous; class III, slightly hazardous; class U, unlikely to pose an acute hazard in normal use; NA: not available. Label instructions must always be followed when using insecticides.

ae The strength of the finished formulation when applied depends on the performance of the spraying equipment used.

Box 24: Example of monitoring and evaluation of space spray and secondary transmission of DF/DHF[af]

Evaluation of timeliness, coverage and effectiveness of space spray for DF/DHF control were evaluated using the geographical information system (GIS) and an attempt was made to describe the spatial-time patterns of DF/DHF secondary case. A longitudinal monitoring of DF/DHF cases and spray activities in Songkhla municipality in Thailand was conducted. After a case was detected, subsequent cases occurring within a radius of 100 metres from the venue of the case up to a period of between 16 and 35 days were considered potential secondary cases. Poisson regression was used to identify risk factors for the secondary attack during the period May 2006–April 2007.

In the study period, 140 cases residing in Songkhla municipality were detected. Of these, 25 were potential secondary cases contracted from 20 index cases. Where combine secondary cases occurred, the mean secondary attack rate was 2.7 per 1000 population. Houses in the neighbourhood of all the index cases were sprayed, but only once. The median lag time of spray was 17.3 hours. Average percentage of the total area sprayed was 5.6%. It was concluded that space spray in the study area was inadequate and often failed to prevent secondary cases of DF/DHF. Further investigation with a larger sample was, however, underscored.

For effective space spray for DF/DHF outbreak control, increasing the spray area to cover a radius of 100 metres from the patient's house and doubling the time of spray at an interval of every seven to ten days in addition to a control programme focusing on the houses of the poorer sections of the community was suggested.

The use of insecticides for the prevention and control of dengue vectors should be integrated into environmental methods wherever possible. During periods of little or no dengue virus activity, the routine source reduction measures described earlier can be integrated into the larvicide application processes in containers that cannot be eliminated, covered, filled or otherwise managed.

For emergency control to suppress a dengue virus epidemic or to prevent an imminent outbreak, a programme of rapid and massive destruction of the *Ae. aegypti* population should be undertaken involving both insecticides and source reduction and using the techniques described in these guidelines in an integrated manner.

Preparedness for minimizing magnitude of transmission during seasonal peaks

There is an opportunity for targeted dengue control since endemic countries are aware of their seasonal peak dengue transmission periods. Efforts should be made to take pre-emptive action to minimize the magnitude of dengue transmission during this period. These pre-emptive actions, focusing on source reduction, should begin as early as up to four months ahead of the seasonal peak to first cover areas demonstrating lower to higher risk of dengue transmission. The areas at higher risk of dengue transmission should be covered at least a month before the seasonal peak.[ag]

An example of such a preparedness programme in Singapore is presented in *Box 25*.[ah]

af Suwich T. et al.: Space Spray and Secondary Transmission of DF/DHF in an Urban Area, Southern Thailand. (Manusript)

ag For additional information refer to section on "Outbreak Response" in the Asia-Pacific Dengue Strategic Plan (2008–2015) and Chapter 13 of this document.

ah Source: National Environment Agency, Singapore, 2009.

Box 25: Preparedness programme in Singapore

To reduce dengue transmission Singapore has adopted an integrated evidence-based approach. This comprises vector surveillance and control, intersectoral collaboration, public education and community outreach, law enforcement and research. The approach is reviewed periodically to ensure its relevance and effectiveness in addressing new challenges which arise from a number of factors including changing dengue serotypes, *Aedes* mosquito adaptation, transboundary transmission, low herd immunity, increasing population density and rapid urbanization.

Before to the beginning of each year, areas at potential risk for dengue outbreaks are identified for intensive source reduction exercises (ISRE) to be conducted two months before the traditional dengue season, which falls between May and October. Based on this risk assessment, resources for vector control operations are deployed in a targeted manner to achieve maximum impact.

In addition to the ISRE, through intersectoral collaboration the various land agencies will also be alerted to conduct intensive source reduction exercises on their properties. The public is also regularly reminded about the need for preparedness against dengue through outreach initiatives on different local media and through community events at the grassroots level. This helps to keep the subject of dengue fresh and the public on alert.

By taking a proactive stance with a preparedness programme, this integrated evidence-based approach has been successful in curbing the spread of dengue in Singapore. The dengue situations in 2008 and 2009 have shown downward trends: from 7031 cases in 2008 to 4497 in 2009. This is in sharp contrast with a high of 14 209 cases reported during Singapore's worst ever dengue outbreak in 2005. This is the first time in three decades that such a downward trend has been observed in Singapore notwithstanding the global surge in dengue cases.

9.4 Geographical information system for planning, implementation and evaluation

The geographical information system (GIS) is an automated computer-based system with the ability to capture, retrieve, manage, display and analyse large quantities of spatial and temporal data in a geographical context. The system comprises hardware (computer and printer), software (GIS software), digitized base maps, information and a whole set of procedures such as data collection, management and updating.

Specific diseases and public health resources can be mapped in relation to their surrounding environment and existing health and social infrastructures. Such information when mapped together creates a powerful tool for monitoring and management of disease. GIS provides a graphical analysis of epidemiological indicators over time, captures spatial distribution and severity of the disease, identifies trends and patterns, and indicates if and where there is a need to target extra resources. Various potential usages and constraints of GIS for dengue control were described by a Scientific Working Group on Dengue in 2006.[135]

Potential usages of GIS technology in dengue control programme

GIS technology could be used to improve dengue control programmes in the following ways:

- GIS technology improves the ability of programme staff, planners, decision-makers and researchers to organize and link datasets (e.g. by using geocoded addresses, geographical boundaries or location coordinates) from different sources.

- GIS, global positioning system (GPS) and remote sensing (RS) technologies provide dengue programme staff with additional types of data such as latitude-longitude coordinates for locations of breeding sites, and cases and transmission sources according to house lot, block and neighbourhood. Digital imagery from satellites and aerial photographs provide additional details to the map and improve the accuracy of the information.
- GIS technology encourages the formation of data partnerships and data sharing at the community level.
- Spatial analysis capability of GIS (distance, proximity, containment measures) can be used to improve entomological/vector control activities and interventions such as focal treatment, and to search for and destroy transmission sources.
- GIS technology enables work on multiple scales in space and other dimensions (time, individual and aggregated data).
- GIS capabilities for spatial and spatial–temporal statistical analysis can improve the information system by providing better support to planning, monitoring, evaluation and decision-making in the dengue control programme.
- GIS capability allows for synthesizing and visualizing information in maps.

Constraints of GIS technology in the context of dengue control

Some of the constraints of GIS technology from the dengue control programme perspective are mentioned below:

- GIS technology is not yet a common tool in vector control programmes. In fact, few GIS applications can be found for the control of dengue and other vector-borne diseases.
- Accurate, low-cost street maps and other cartographic databases such as of neighbourhood, block and house lot boundaries are essential for dengue control programmes. Some of these maps can be accessed through the Internet.
- Professionals, planners, technicians and especially state/departmental/provincial and local dengue control programme staff need training and user support in GIS technology, data and epidemiological methods in order to use the technology appropriately and effectively.
- The cost of commercial GIS software is a barrier to extending the use and development of GIS applications in public health and, particularly, in dengue control programmes. However, in recent times, more GIS software, which could be accessed at no cost, is becoming increasingly available through the Internet.

Field applications of GIS for dengue control: Case studies

Use of GIS for dengue control in Singapore

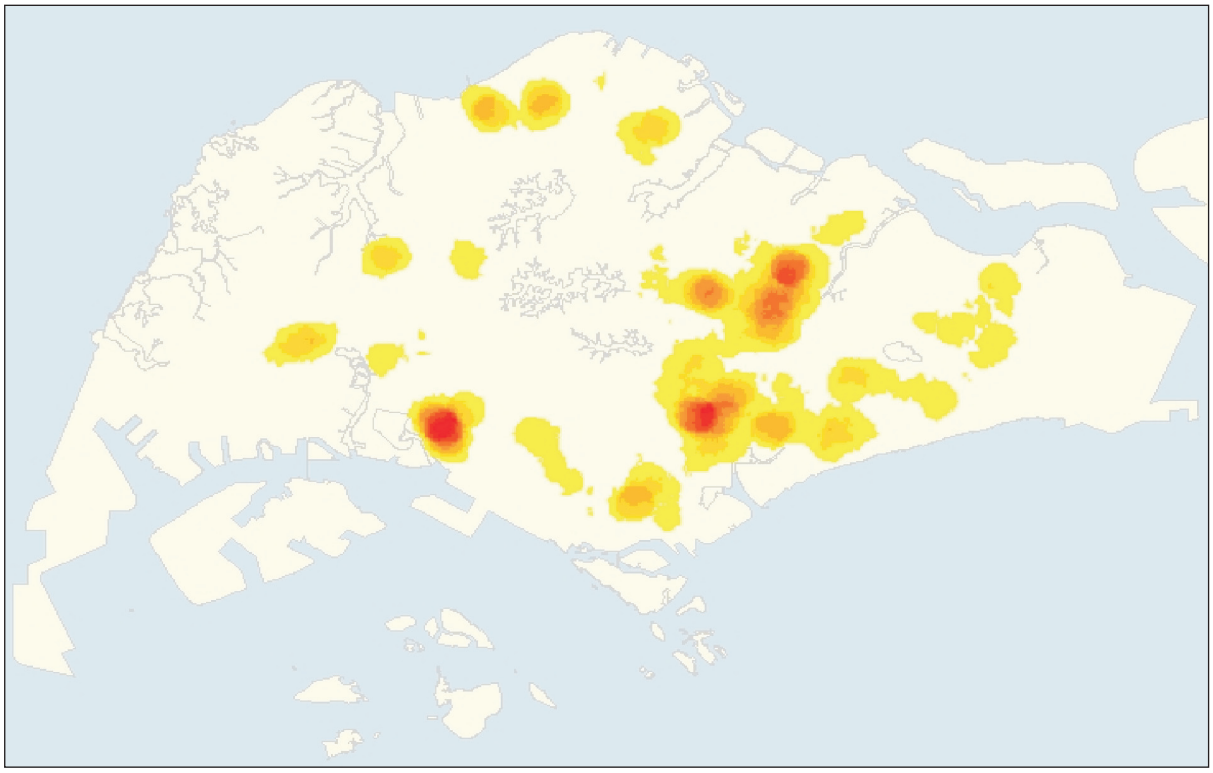
- Ovitraps are used extensively in Singapore[136] as a tool to monitor, detect and control *Aedes* populations. They give an approximate measure of the adult population in an area and act as an early warning signal to pre-empt any impending dengue outbreaks. A GIS was established in 1998 to develop a real-time *Aedes* mosquito control and monitoring system for spatial epidemiological study.

  The GIS monitors the network of 2000 ovitraps placed island-wide to better understand vector trends and disease patterns. Analysis is done on the ovitrap breeding data collected weekly to identify hotspots and risk areas where there is a danger of high *Ae. aegypti* infestation. Three ovitrap models have been developed to analyse the ovitrap breeding data. The analysis results are used to plan vector surveillance and control operations. Subsequently, an improved approach of GIS was applied that included spatial identification

of "hot spots" by using hand-held terminals (HHT) for collection of field surveillance data in the field itself,[137] unlike the previous approach of collecting information on paper forms in the field and then feeding the same into the computer for analysis.

- Currently, Singapore uses GIS in its dengue surveillance and control programme to process, map and analyse huge amounts of epidemiological, entomological and environmental data.[138] A fully automated dengue model is run daily using GIS to conduct spatial and temporal analysis of the dengue cases (*Figure 14*). With this information, swift vector control action can be taken to prevent further dengue transmission within the affected area.

Figure 14: Density mapping of dengue cases in Singapore

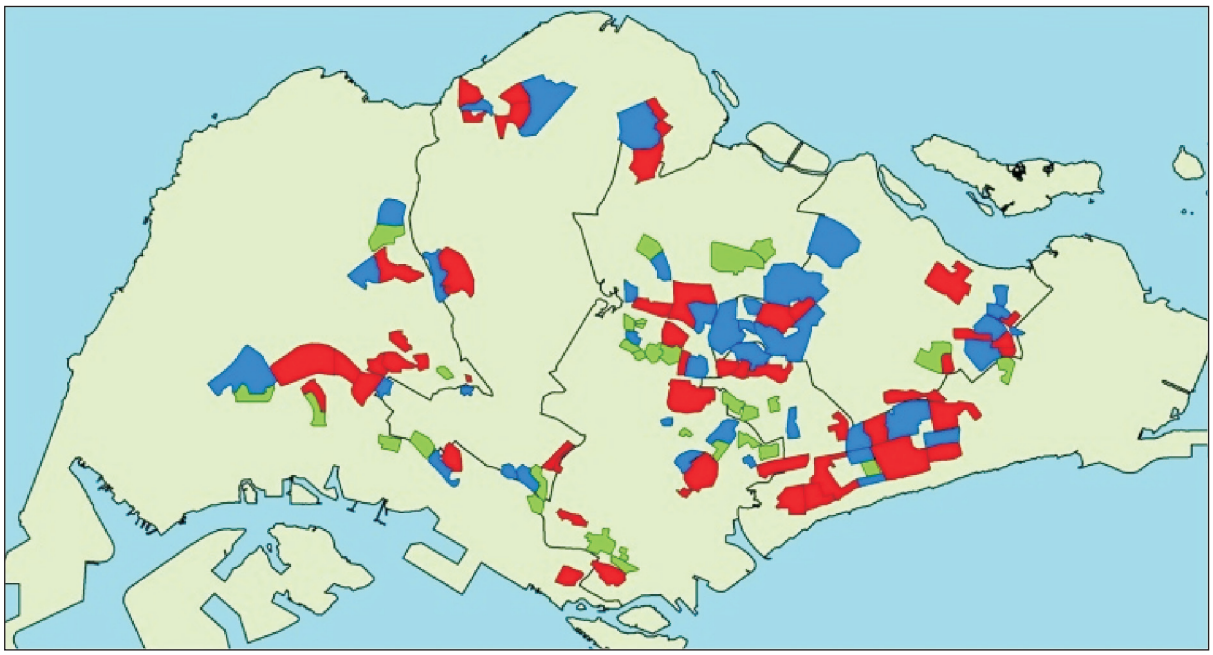


Source: National Environment Agency, Singapore, 2009.[139]

Through the use of GIS, the distribution of *Aedes* mosquitoes breeding, dengue cases, dengue serotypes and environmental factors such as construction sites, vacant premises and congregation areas could be monitored and analysed. Risk assessment is conducted to develop areas of potential risk for dengue outbreaks based on the principles of dengue epidemiology and *Aedes* ecology and behaviour.

Taking into consideration the predominant serotype and the population's past exposures to that serotype, the areas identified as having relatively higher epidemic potential are marked out as "focus areas" (*Figure 15*). More resources and intensive vector control will be carried out in these "focus areas", and this information assists the programme managers in their deployment of scarce resources in accordance with the risks and operational needs.

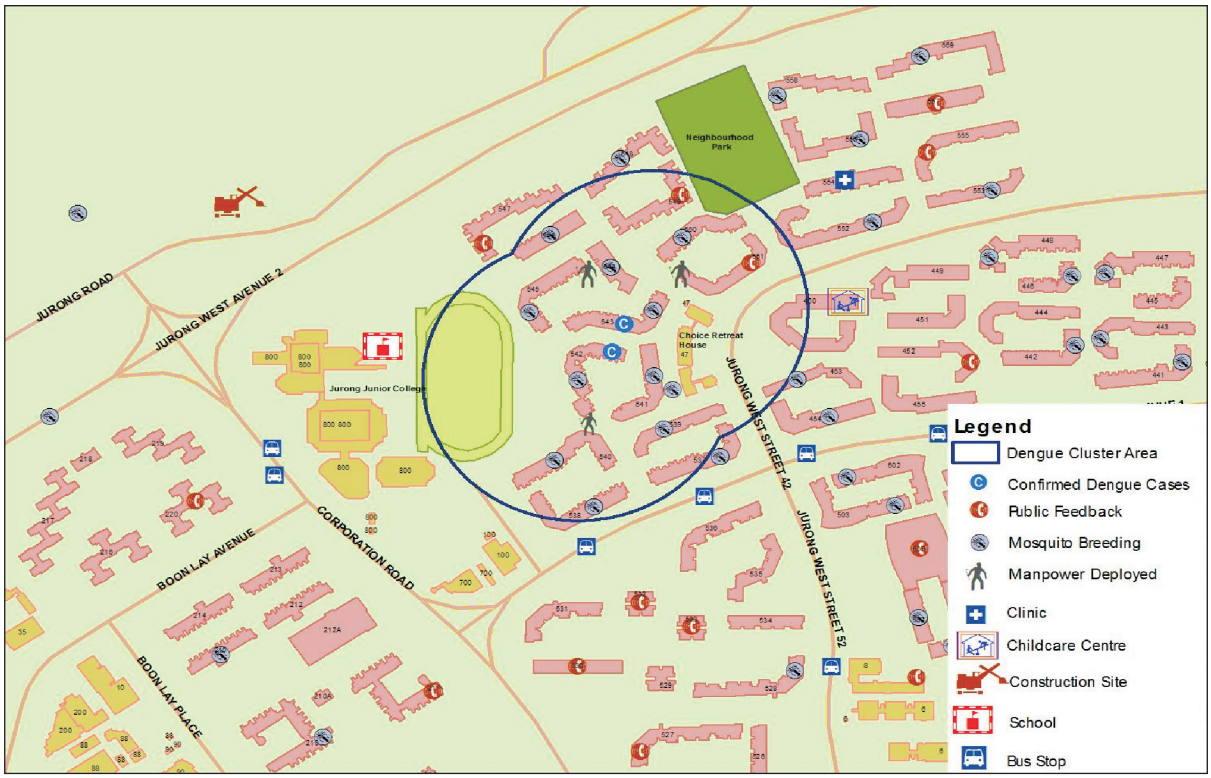
Figure 15: Focus areas identified using GIS to prioritize resource allocation for dengue surveillance



Source: National Environment Agency, Singapore, 2009.[139]

Coupled with the timely availability of information, GIS has been found useful for planning vector control operations, and managing and deploying resources for dengue control (*Figure 16*).

Figure 16: Planning, managing and deploying resources for vector control operations using GIS



Source: National Environment Agency, Singapore, 2009.[139]

Alert system for informing environmental risk of dengue infections

The "Ovitrap Index" has been in use in many countries. This is a measurement of mosquito eggs in specified geographical locations, which in turn reflects the distribution of *Aedine* mosquitoes, the vector for dengue. Using GIS application, an alert system was created from a synthesis of geospatial data on ovitrap indices in Hong Kong. The inter-relationship between ovitrap indices and temperature was established. This forms the rationale behind the generation of weighted overlays to define risk levels. The weighting could be controlled to set the sensitivity of the alert system.

This system can be operated at two levels: one for the general public to assist the evaluation of dengue risk in the community and the other for professionals and academia in support of technical analysis. The alert system offers one objective means to define the risk of dengue in a society, which would not be affected by the incidence of the infection itself.[ai]

Dengue spatial and temporal patterns, French Guiana, 2001

To study a 2001 dengue fever outbreak in Iracoubo, French Guiana, the locations of all patients' homes were recorded along with the dates when symptoms were first observed. A GIS was used to integrate the patient-related information. The Knox test, a classic space-time analysis technique, was used to detect spatiotemporal clustering. Analysis of the relative-risk (RR) variations when space and time distances differed highlighted the maximum space and time extent of a dengue transmission focus.

The results showed that heterogeneity in the RR variations in space and time corresponds to known entomological and epidemiological factors such as the mosquito feeding cycle and host-seeking behaviour. This finding demonstrates the relevance and potential of the use of GIS and spatial statistics in elaborating a dengue fever surveillance strategy.[140]

ai Sze W.N., Yan L.C., Kwan L.M., Shan L.S., Hui L.. An alert system for informing environmental risk of dengue infections. *http://www.iseis.cuhk.edu.hk/eng/research/completed/alert_system.pdf*

10. Integrated Vector Management (IVM)

10.1 Genesis and key elements

Major mosquito-borne diseases in the WHO South-East Asia Region include malaria, dengue, lymphatic filariasis, Japanese encephalitis and kala azar. Each Member country in the past decades had a national control programme for each disease. Subsequently it was realized that due to various technical and operational issues these did not turn out to be cost-effective and that these lacked the coordination and focus required to achieve the expected outcomes. Countries then switched over to the national vector borne disease programmes, since this was not only more cost-effective and efficient but also gave the freedom to programme managers to utilize allocated funds as per the requirements to control a particular disease. Resurgence of malaria, dengue and other vector-borne infections highlighted the need for planning control activities at the micro level on the basis of ecoepidemiological types, which inter alia required the use of old and new proven technologies in tandem.

In 2004, WHO published the *Global Strategic Framework for Integrated Vector Management*.[141] Integrated Vector Management (IVM) entails the use of a range of vector control interventions of proven efficacies through collaborations within the health sector and with other sectors, namely the environment, education, public works department, agriculture and others. Such intersectoral and interprogrammatic approaches improve the efficacy, cost-effectiveness, ecological soundness and sustainability of disease-vector control.

The application of more than one evidence-based or selective intervention in an integrated manner, competent public health legislation, and a sound pesticide management policy are integral to IVM. Through evidence-based decision-making, IVM rationalizes the use of human and financial resources and organizational structures for the control of vector borne disease and emphasizes the engagement of communities to ensure sustainability.

The characteristic features of IVM include:

- **methods based on knowledge of local vector biology, disease transmission and morbidity;**
- **use of a range of interventions, often in combination and synergistically;**
- **collaboration within the health sector and with other public and private sectors that impact vector breeding;**
- **engagement with local communities and other stakeholders; and**
- **a public health regulatory and legislative framework.**

The key elements of IVM are described in *Box 26*.

Box 26: The key elements of IVM

1. Advocacy, awareness generation, social mobilization and legislation:

- Promotion and embedding of IVM principles in the development policies of all relevant agencies, organizations and civil society.
- Establishment of or bolstering regulatory and legislative controls for public health to ensure access to necessary services and health information and communication materials.
- Empowerment of communities and their active participation for advocating local policy changes, resolution of demand-side issues and challenges and inculcating appropriate practices for long-term prevention and control.

2. Collaboration within the health sector and with other sectors:

- Consideration of all options for collaboration within and between public and private sectors, which should be optimal and necessary in times of high alert.
- Application of the principles of subsidiarity in planning and decision-making.
- Necessary capacity-building of partners to address health equity, surveillance, control and prevention of vector-borne diseases.
- Strengthening channels of communication among policy-makers, managers of vector-borne disease control programmes and other IVM partners.
- Mobilization of additional resources, especially at the local levels.

3. Integrated approach:

- Ensuring the rational use of available resources through the application of a multidisease-control approach.
- Integration of non-chemical and chemical vector-control methods.
- Integration with other disease-control measures.
- Establishment of specific integrated bodies/mechanisms to ensure rapid response/action to tackle an outbreak or epidemic.[aj]

4. Evidence-based decision-making:

- Adapting strategies and interventions to local vector ecology, epidemiology and resources.
- Guidance by operational research and routine monitoring and evaluation.
- Information management and research evidence to introduce and advocate for policy change. Local authorities, policy-makers and planning officers should be involved in information management to build ownerships and sustainable response.

5. Capacity-building

- Developing essential physical infrastructure.
- Financial resources and adequate human resources at the national and local level to manage IVM programmes based on situation analysis/needs assessments.

aj A "Disease Control Task Force led by community/area-based CDC"; a "Health promotion and preventive medicine unit in the Primary Health Care Unit"; a "Community Task Force" led by full participation of people who are empowered with technical support from the health sectors; a "community surveillance mechanism" which can be used in other health alert systems as an integral part of vector-borne disease control.

The SEA Regional IVM Strategy recommended IVM approval for malaria, dengue and kala azar control.[142] This was prompted by promising results achieved in malaria control in Sri Lanka by empowering communities through the involvement of *"Farmers' Field Schools"*.[143]

10.2 Approach

The urban and peri-urban eco-epidemiological paradigm is home to vectors of dengue and chikungunya, where they proliferate in diverse types of water-storage containers both indoors and outdoors (see *Chapter 8*).

The IVM approach for dengue control is a classic example of multiple disease control, thus making control of three infections (namely. dengue, chikungunya and urban malaria) possible in a most cost-effective manner.[ak] For example, in the Indian subcontinent, urban malaria transmitted by *Anopheles stephensi* is also endemic. *An. stephensi*, also being a container habitat species, shares breeding sites with *Ae. aegypti*.

However, the urban disease control programme suffers from lack of: (i) social mobilization of communities; (ii) intersectoral coordination; (iii) public health infrastructure (especially experts in vector ecology for mapping of breeding sites and for selection of appropriate mix of interventions); (iv) capacity-building; (v) administrative, financial and logistic support; and (vi) monitoring and evaluation.

Over the last few decades, efforts to promote community-oriented activities for dengue control in an IVM mode have increased. A comprehensive review of community-based programmes for dengue control[144] was carried out. The review found a tangible need to strengthen such programmes. The essential steps to improve the outcome and sustainability of control activities on a long-term basis are described below.

Community participation

Community participation has been defined "as a process whereby individuals, families and communities are involved in the planning and conduct of local vector control activities so as to ensure that the programme meets the local needs and priorities of the people who live in the community, and promotes the community's self-reliance in respect to development".[145] In short, community participation entails the creation of opportunities that enable all members of the community and extended society to actively contribute to it, influence its development, and share equitably the fruits of accrued benefits. The objectives of community participation in dengue prevention and control are to:

- Extend the coverage of the programme to the whole community by creating community awareness. This, however, often requires intensive inputs.
- Make the programme more efficient and cost-effective, with greater coordination of resources, activities and efforts pooled by the community.
- Make the programme more effective through joint community efforts to set goals, objectives and strategies for action.
- Promote equity through the sharing of responsibility, and through solidarity in serving those in greatest need and at greatest risk.
- Promote self reliance and self-care among community members and increase their sense of control over their own health and destiny.

ak More details can be seen in the *Report of the WHO Consultation on Integrated Vector Management,* Geneva, 1–4 May 2007.1462

Community participation approaches

- ***By showing concern:*** Community and government organizers should reflect true concern for human suffering, i.e. in this case morbidity and mortality due to dengue in the country, economic loss to families and the nation on account of it, and how the benefits of the dengue prevention and control programme fit into the people's needs and expectations.
- ***Initiating dialogue:*** Community organizers and opinion leaders or other key personnel in the power structure of the community, namely women's groups, youth groups and civic organizations, should be identified. Dialogue should be carried out through personal contacts, group discussions and film/audiovisual shows, etc. Interaction should generate mutual understanding, trust and confidence, enthusiasm and motivation. The interaction should not be a one-time affair but should be a continuing dialogue to achieve sustainability.
- ***Creating community ownership:*** Organizers should use community ideas and participation to initiate the programme, community leaders to assist the programme, and community resources to fund the programme. The partnership of the community with mosquito control and abatement agencies should be strong and the latter should provide technical guidance and expertise.
- ***Health education (HE):*** Health education should not be based on telling people the do's and don'ts through a vertical, top-down communication process. Instead, health education should be based on formative research to identify what is important to the community and should be implemented at three levels, i.e. the community level, the systems level and the political level.
- ***Community level:*** People should not only be provided with knowledge and skills on vector control, but relevant educational material should empower them with the knowledge that allows them to make positive health choices and gives them the ability to act individually and collectively. A participatory approach in community health communication is imperative.
- ***Systems level:*** To enable people to mobilize local action and social forces beyond a single community, i.e. health, development and social services.
- ***Political level:*** Mechanisms must be made available to allow people to articulate their health priorities to political authorities. This will facilitate placing vector control high on the priority agenda and effectively lobby for suitable policies and actions.
- ***Defining community actions:*** The following community actions are essential to sustain DF/DHF prevention and control programmes:
  - At the individual level, encourage each household to adopt routine health measures that will help in the control of DF/DHF, including source reduction and implementation of proper personal protection measures.
  - At the community level, organize "clean-up" campaigns two or more times a year to control the larval habitats of the vectors in public and private areas of the community. Some key factors for the success of such campaigns include: extensive publicity via media-mix including audiovisuals, posters, pamphlets, etc.; and proper planning, pre-campaign evaluation of foci, execution in the community as promised, and follow-up evaluations. Participation by municipal/public sector sanitation services and agencies should be ensured.
  - Where community-wide participation is difficult to arrange for geographical, occupational or demographic reasons, arrange community participation through nongovernmental/voluntary/community-based/faith-based associations and organizations. The people in these organizations may interact daily at work or institutional settings, or come

together for special purposes, i.e. religious activities, civic clubs, women's groups and schools, etc.

- Emphasize school-based programmes targeting children and parents to eliminate vector breeding at home and at school.
- Challenge and encourage the private sector to participate in the beautification and sanitary improvement of the community as sponsors, emphasizing source reduction of dengue vectors.
- Combine community participation in DF/DHF prevention and control with other priorities of community development. Where services such as refuse collection, waste water disposal, provision of potable water, etc. are either lacking or inadequate, the community and its partners can be mobilized to improve such services and at the same time reduce the larval habitats of *Aedes* vectors as part of an overall effort at community development.
- Combine dengue vector control with the control of all species of disease-bearing and nuisance mosquitoes as well as other vermin, to ensure greater benefits for the community, and consequently greater participation in neighbourhood campaigns.
- Arrange novel incentives and/or service recognition programmes for those who participate in community programmes for dengue control. For example, a nationwide competition can be promoted to identify the cleanest communities or those with the lowest larval indices within an urban area.

Over the years, community participation in controlling dengue vector is being increasingly applied in many countries. *Box 27* illustrates an example of how dengue prevention and control in Indonesia has evolved from a vertical, government-controlled programme to a more horizontal, community-based approach.

Model development

Development of a model for dengue control through the community participation approach should be initiated in order to define potential prime-movers in the communities and to study ways to persuade them to participate in vector control activities. Social, economic and cultural factors that promote or discourage the participation of these groups should be intensively studied to enhance participation from the community. Mapping of community resources and infrastructure physically and socially would help shape up the model development for dengue control. Mapping will also identify key change agents that mobilize communities to change their behaviour towards and compliance of vector-borne disease control.

Different models in different settings should be applied:

- In rural areas, where an acute sense of community exists, community participation is needed and has to be encouraged in addition to training and capacity-building.
- In urban and semi-urban areas, civil society groups, nongovernmental organizations and municipalities can act as prime movers for change and need to be mobilized to involve the community.

Model development focusing on schoolchildren has been studied in several countries (*Box 28*) and this strategy should be modified and introduced in each country.

Box 27: 'Together Picket': Community activities in dengue source reduction in Purwokerto city, Central Java, Indonesia[146]

In Purwokerto, Central Java, Indonesia, a partnership has been established between the local government, the Rotary Club, the Family Welfare Empowerment Organization (PKK), and municipal health services. Leadership and commitment from these partners, with strong technical support from the National Health Research Department, has enabled the development of an effective community-based integrated vector control project in Purwokerto, which has a population of 220 000.

This project operates at the level of neighbourhood associations. Each neighbourhood consists of between 25 and 50 households. Within each neighbourhood, houses are grouped into sets of 10, called "*dasawisma*". Each *dasawisma* has a leader, usually a woman cadre from the PKK, trained in DF/DHF prevention and control. The leader is known as the "source reduction cadre". Usually, being bestowed this title itself is an honour to be proud of. Each *dasawisma* gets a "source reduction kit" containing a flashlight (for checking for the presence of larva in containers stored in dark areas), simple record forms, and a health education booklet. The *dasawisma* arrange schedules within which one house inspects the other nine houses. Known as "*Piket Bersama*" ("Picket Together"), these house-to-house inspections are conducted on a weekly basis so that each household takes its turn every 10 weeks.

The *dasawisma* leader collects the weekly record forms and reports the results to the next administrative level. The success of this project can be measured by the reduction in the House Index from 20% before activities began to 2% once the activities were on a roll. This project has now been expanded to 14 cities in Indonesia through grants from the Rotary International and CDC, Colorado.

Box 28: Health education in elementary school[147]

A child-focused approach to dengue prevention and control has been an important component of a broader public health programme in Puerto Rico since 1985. The highlights include health education in elementary schools with collaboration between the departments of Health and Education, among other initiatives.

In elementary schools, an activity booklet was developed that contained 28 activities about dengue and its prevention and was accompanied by a guide to aid teachers in the presentation of the various activities. After several years of use and following suggestions from teachers and external programme reviewers, the booklet and teacher's guides were revised. Each year, an estimated 50 000 fourth-grade students use the booklet in their social studies classes and it has now been incorporated into the public school curriculum. An important aspect of this programme has been the provision of training programmes for teachers, school nurses and school nurse supervisors by staff of the Center for Disease Control and Prevention, Puerto Rico.

Social mobilization

Advocacy meetings should be conducted for policy-makers for garnering political commitment to mass clean-up campaigns and environmental sanitation. Intersectoral coordination meetings should be conducted to explore possible donors/partners for mass antilarval control campaigns and

measures and to help finance the programme. Reorientation training of health workers should be conducted to improve their technical capability, and their ability to supervise prevention and control activities. A "DF/DHF month" should be identified twice a year, during the pre-transmission and peak transmission period.

Health education

Health education is very important in achieving community participation. It is a long-term process to achieve human behavioural change, and thus should be carried out on a continuous basis.[al] Though countries may have limited resources, health education should be given priority in endemic areas and in areas at high risk for DF/DHF. Health education is conducted through the channels of interpersonal communication, group educational activities, mid-media activities such as wall writing, and mass media broadcasts.

Health education can be implemented by women's groups, school teachers, formal and informal community leaders, and health workers/volunteer networks. Health education efforts should be intensified before the period of dengue transmission as one of the components of social mobilization. The main target groups are school children, women and other "influencers" at the community level in addition to the community in general.

Intersectoral coordination

Developing economies in the South-East Asia Region have identified many social, economic and environmental problems that promote mosquito breeding. The dengue control issue thus exceeds the capabilities of the ministries of health. The prevention and control of dengue requires collaboration and partnerships between the health and non-health sectors (both government and private), nongovernmental organizations (NGOs) and local communities.

During epidemics such cooperation becomes even more critical since it requires the pooling of resources from all groups to check the spread of the disease. Intersectoral cooperation involves at least two components:

- Resource sharing.
- Policy adjustments and activities among various ministries and nongovernment sectors.

Resource sharing:

Resource sharing should be sought wherever the dengue control coordinator can make use of underutilized human resources, e.g. for local manufacture of required tools, seasonal government labourers for water supply improvement activities, or community and youth groups to clean up discarded tyres and containers in neighbourhoods.

The dengue control programme should seek the accommodation or adjustment of existing policies and practices of other ministries, sectors and municipal governments to incorporate public health as a central focus of their goals. For instance, the public works sector could be encouraged to accord first priority to water supply improvements for communities at the highest risk of dengue. In return, the Ministry of Health could consider authorization of the use of some of its field staff to assist the ministry responsible for public works to repair water supply and sewerage systems, as appropriate.

al Refer to Chapter 12 for additional details (Communication for Behavioural Impact) on responsive behaviour within an enabling environment.

Activities by government ministries/departments and NGOs

The role of the ministry(ies)/department(s)/municipalities responsible for public works/roads and the buildings sector:

The key roles to be performed by these sectors pertaining to dengue prevention and control include: reduction at source (storage containers) by providing a safe and dependable water supply, adequate sanitation, and effective solid waste management. 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 supplies or sewerage connections and rainwater (storm water) run-off control for new housing developments, or forbid open surface wells as well as formulate or update public health by-laws. During the construction of roads and buildings, efforts need to be made to merge pits by breaking bunds, making excavations in line with the natural slope or gradient and making arrangements for the water to flow into natural depressions, ponds or rivers. Follow-up action after each excavation is also critical.

The role of the ministry/department responsible for water supply:

The key roles for this ministry/department pertaining to dengue prevention and control include: repair of leakages to prevent pooling of water, restoration of taps, diversion of waste water to ponds/ pits, staggering of water supply, mosquito-proofing of water harvesting devices and repair of sluice valves.

Role of the ministry/department responsible for urban development:

The key roles for this ministry/department pertaining to dengue prevention and control include: implementation of building by-laws, improved designs to avoid undue waterlogging, securing correct building use permission after clearance by the health department.

***Role of the ministry/ department responsible for education*:**

The Ministry of Health should work closely with the Ministry of Education to develop a health education (health communication) component targeted at schoolchildren that will design and communicate appropriate health messages. Health education models can be jointly developed, tested, implemented and evaluated for various age groups.

Research programmes 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 supply, educational interventions to promote community sanitation, waste characterization studies) to dengue control programmes.

Role of the ministry/department responsible for environment/forests:

The Ministry of Environment can help the Ministry of Health collect data and information on ecosystems and habitats in or around cities at high risk of dengue. Data and information on local geology and climate, land usage, forest cover, surface water and human populations are useful in planning control measures for specific ecosystems and habitats.

The Ministry of Environment may also be helpful in determining the beneficial and adverse impacts of various *Ae. aegypti* control tactics (chemical, environmental and biological). These may include appropriate environment management policies and pesticide management policies. Other roles could be the reclamation of swampy areas and social forestry.

Role of the ministry/department responsible for information, communication and mass media:

Information directed at the community at large is best achieved through the media/channel-mix, including such mass media as television, radio and newspapers. Therefore, the ministry responsible for information, communication and the mass media should be approached to coordinate the release of messages on the prevention and control of dengue developed by public health specialists.

Role of the ministry/department responsible for water resources:

The key roles for this ministry/department pertaining to dengue prevention and control include development and maintenance of a canal system, intermittent irrigation, design modifications and lining of canals, weeding for proper flow, creating small check-dams away from human settlements and health impact assessment (HIA).

Role of the ministry/department responsible for industry/mining:

The key roles for this ministry/department pertaining to dengue prevention and control include improving drainage/sewerage systems, safe disposal of solid waste/used containers, mosquito-proofing of dwellings, safe water storage/disposal and use of ITN/ LLIN. Other roles may include: R&D in relation to the development of new, safer and more effective insecticides/formulations, and promoting safe use of public health pesticides.

Role of the ministry/department responsible for agriculture:

The key roles for this ministry/department pertaining to dengue prevention and control include the utilization of Farmers' Field Schools to implement IVM, popularizing the concept of dry-wet irrigation through extension education, and pesticide management.

Role of the ministry/department responsible for fisheries:

The key roles for this ministry/department pertaining to dengue prevention and control include institutional help/training in mass production of larvivorous fish, and the promotion of composite fish farming schemes at the community level.

Role of the ministry/department responsible for railways:

The key roles for this ministry/department pertaining to dengue prevention and control include proper excavations, maintenance of yards and dumps and anti-larval activities within their jurisdiction, and HIA for health safeguards.

Role of the ministry/department responsible for remote sensing/GIS:

The key roles with regard to remote sensing and GIS pertaining to dengue prevention and control include technical support and training in mapping environmental changes and disease risks using GIS.

Role of the ministry/department responsible for planning:

The key roles for this ministry/department pertaining to dengue prevention and control include the active involvement of health authorities at the planning stage for HIA and the incorporation of appropriate mitigating actions in development projects.

Role of nongovernmental organizations (NGOs):

NGOs can play an important role in promoting community organization and mobilization for implementing environmental management for dengue vector control and to improve health-seeking behaviour. This will most often involve health education, source reduction and improvement of housing related to vector control. Community NGOs may be informal neighbourhood groups or formal private voluntary organizations, service clubs, churches or other religious groups, as well as environmental and social action groups.

After adequate training on source reduction methods is provided by the Ministry of Health staff, NGOs can contribute actively by collecting discarded containers (tyres, bottles, tins, etc.), cleaning drains and culverts, filling depressions, removing abandoned cars and roadside junk, and distributing sand or cement to fill tree holes. NGOs may play a key role in developing a regimen of recycling activity to remove discarded containers from yards and streets. Such activities must be coordinated with the environmental sanitation service.

NGOs may also be able to play a specific, but as yet not fully explored, role in environmental management during epidemic control. With guidance from the Ministry of Health, NGOs could concentrate on the physical control of locally identified, key breeding sites such as water drums, accumulated waste tyres and cemetery flower vases. The NGOs can be involved in village-level training, distribution of BCC/IEC materials, and ITN promotion and distribution.

Clubs such as Rotary International have supported DF/DHF prevention and control programmes in the American Region for over 15 years. In Asia and the Pacific, programmes have been initiated by them in Sri Lanka, Philippines, Indonesia and Australia to provide economic and political support for successful community-based campaigns. A new grant from the Rotary Foundation has been made to study the possibility of upscaling this project to a global programme.

Women's clubs and associations in many countries have contributed to *Ae. aegypti* control by conducting household inspections for foci and carrying out source reduction. There are many opportunities, mostly untapped, for environmental organizations and religious groups to play similar roles in *Ae. aegypti*-infested communities.

Legislative support

Legislative support is essential for the success of dengue control programmes. Many countries in the SEA Region have formulated and enacted legislation to address the control of epidemic diseases which authorize health officers to take necessary action within the community for the control of epidemics. Some municipalities/local governments have also adopted legislative provisions related to dengue control.

All Member countries of the SEA Region are signatories to the International Health Regulations (IHR) 2005. These Regulations have a specific provision for the control of *Ae. aegypti* and other disease vectors at sea/air/land entry points.

The formulation of legislation on dengue/*Ae. aegypti* control should take into consideration the following points:

- Legislation should be a necessary component of all dengue/*Ae. aegypti* prevention and control programmes. Dengue should be made a notifiable disease.
- Legislation should cover all aspects of environmental sanitation in order to effectively contribute to the prevention of all transmissible diseases and should aim at developing human resources within the institutional framework. In countries where sanitary regulations are primarily the responsibility of agencies other than the Ministry of Health, there should be coordinated plan of action with all the ministries and agencies concerned.

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

10.3 IVM implementation

IVM implementation should thus begin with situational analysis (epidemiological, entomological, insecticide resistance status, pesticide management, policy frameworks) and vector control needs assessment (related to healthy public policy, and technical, financial and operational needs). The next major steps are setting goals and objectives, selecting priority diseases for integrated action, appropriate decision-making regarding the application of IVM and choosing appropriate interventions, stratification of targeted area(s) [macro/micro-stratification by paradigms, terrain/accessibility, epidemiological, entomological, ecological and socio-anthropological factors, development activities and drug-resistance areas].

Further implementation steps should include advocacy and intersectoral collaboration within health and other sectors; communication and social mobilization using the COMBI approach;[am] capacity-building and training that improves vector control knowledge and skills; and building institutional capacity as well as facilitating capacity-building of other sectors.[148]

10.4 IVM monitoring and evaluation

Monitoring and evaluation are essential components of IVM. Monitoring measures the implementation of its range of activities (the process), while evaluation measures the extent to which direct outcomes have been achieved. Impact assessment determines the effects or the impact attributable to the programme. The inputs and processes required to deliver each activity or intervention, and their relative contribution to the overall impact, must be assessed for effectiveness, cost-effectiveness and sustainability in a given situation. Regular supportive supervision with a standardized checklist should be an important element.

A sound monitoring and evaluation system involving suitable input, process, output, outcome, impact indicators and targets should be set as per local requirements, especially in the case of community empowerment and multisectoral action. The involvement of partners and community representatives in participatory evaluation is important because it increases programme ownership and has the potential to generate data on behavioural, social and political changes that would be difficult to obtain through interviews.

Operational research should also be a priority. A number of issues will need scientific examination to develop feasible, cost-effective, socially acceptable and thus sustainable interventions for each local eco-epidemiological setting/stratum. Monitoring and evaluation can be considered a part of operational research in the context of IVM since the outcomes will enable improvement of inputs and implementation processes. The operational research issues will be identified for each district. Some of the key areas may include KABP surveys to determine community acceptance of interventions, evaluation of effectiveness of IVM programme, insecticide resistance monitoring, and evaluation of new vector control intervention methods, etc.[148]

10.5 Budgeting

Like any other plan, the IVM implementation plan also will require an estimation of the resources required and then a budget covering all possible anticipated activities and keeping the time frame in mind.[148]

am Refer to Chapter 12 for additional infomation.

11. Communication for Behavioural Impact (COMBI)

In the absence of vaccines and drugs, the strategies for the prevention and control of dengue include prompt diagnosis of fever cases, providing appropriate clinical management, and reducing human-vector contact through vector control and personal protection methods. For effective reduction of human-vector contact, particular emphasis has to be placed on the management or elimination of larval habitats in and around homes, work settings, schools, and in other less obvious places such as informal dump-sites and playgrounds.[an] Community awareness generation and community and intersectoral participation in addition to disease and vector surveillance, emergency preparedness, capacity-building and training, and research are essential ingredients of prevention and control efforts.

Though carefully researched and meticulously planned advocacy, mobilization and communication initiatives with high levels of community engagement are recognized as fundamental to the promotion of healthy behaviour and social change, yet till date few national DF/DHF programmes and international funding agencies have invested soundly in such initiatives.[149,ao] Adequate prevention and control methods exist, but many national programmes are unable to deliver them effectively.[150,ap] Many programmes struggle to achieve and sustain behavioural impact at the household, workplace, urban planning, and policy levels.[130,151–157,aq] Further, translation of knowledge to practice often varies.[157–164] This is on account of reasons as diverse as lack of resources, irregular application and ineffectiveness of methods/interventions for vector control that have been promoted (example, methods promoted for cleaning water containers).[165,166] Even with good levels of knowledge, people may resist household or personal practices to control the vector and view such actions to be the responsibility of the government.[167,168]

In addition, people do not change their behaviour all of a sudden and stay the "changed" way from that moment. Instead, people's behaviour gradually moves through subtle stages of change: from becoming aware to becoming informed, then becoming convinced, followed by the decision to take action, then the actual taking of relevant action the first time, then repeating the same, and finally maintaining that action (*Box 29*) continuously.

an WHO. Report of the Consultation on: key issues in dengue vector control, toward the operationalization of a global strategy, CTD/FIL(DEN)/IC/96.1, 2001. *http://www.who.int/emc-documents/dengue/docs/whocdsdenic20001.pdf*

ao Cited from: Parks, *et al*. International Experiences in Social Mobilization and Communication for Dengue Prevention and Control. *Dengue Bulletin – Vol 28, 2004 (Suppl.)*: 1-7.

ap ibid.

aq ibid.

Box 29: HICDARM and Behaviour Adoption[ar]	
First, we Then, we become And later	**H** ear about the new behaviour. **I** nformed about it. **C** onvinced that it is worthwhile.
In time, We make the And later we take We next await and if all is well, we	 **D** ecision to do something about our conviction. **A** ction on the new behaviour. **R** e-confirmation that our action was good. **M** aintain the behaviour!

Most programmes usually manage to increase awareness and inform, educate and convince individuals about what needs to be done (the HIC phase). Prompting people to take the necessary steps towards adopting and maintaining an effective and feasible new behaviour (the DARM phase) remains a challenge.

Human recall is very short: communities may actively respond to a "crisis situation" but once that phase is over they tend to retire into the restive phase. Hence, the success and sustainability of the programmes depend upon continued motivation and mobilization of communities, till the threat of disease (for example, DF/DHF) exists.

Constraints in various community-based prevention programmes in general have been documented.[169] Major constraints identified to come in the way of achieving modest success in community-based programmes include the following:

- Designs have a strong educational component but without the motivational elements that set off community participation and inculcate a sense of ownership.
- Insufficient and intermittent efforts and inadequate resources.
- Inadequate intersectoral convergence in terms of time and resource sharing.
- Indifferent attitude of the upper strata of society wherein there is the inherent belief that dengue control is the responsibility of the government, and that the urban poor, who are mostly illiterate and too busy securing the minimum daily earnings, can perhaps live with the presence of mosquitoes.
- Security concerns and inconvenience caused often prevent the entry of health workers into households.
- Prevailing superstitions, beliefs and faiths [for example, children suffering from AIDS, malaria and other diseases are prime targets of witchcraft accusations, in Angola.[170] Once accused of practising witchcraft, a child is punished, beaten, starved and sometimes killed to "cleanse" her or him of supposed magical powers].

Kyle and Harris[30] summed up the performance of community-based programmes saying that the key to promote such programmes is to close the motivational gap between the community's knowledge and sustainable practices (namely reducing mosquito breeding sites).

The rationale for community-based health promotion is the notion that individuals cannot be considered separately from their social milieu and context and that programmes incorporating multiple interventions extending beyond the individual level have the potential to be more successful in the context of changing behaviours.[171,172]

ar ©Hosein, E. (cited from: Parks W., Lloyd L.. Planning Social Mobilization and Communication for Dengue Fever Prevention and Control: A step-by-step guide. WHO, Geneva 2004 (WHO/CDS/WMC/2004.2 and TDR/STR/SEB/DEN/04.1).

It is only during the last decade that emphasis on a community-based integrated approach ("bottom up" rather than "top down") started gaining attention,[130] moving away from the biomedical approach, although change is often resisted.[as] The supportive activities included an understanding of prevalent knowledge, attitudes and practices (KAP) and the development and dissemination of material related to information, education and communication (IEC) focusing mostly on prevention-oriented messages towards actions taken to be taken by the communities.

Since then, there is a growing body of evidence to prove that social mobilization and communication are critical to sustainable dengue prevention and control. A review of the use of community participation for controlling *Ae. aegypti* via larval source reduction and of the effectiveness and sustainability of programmes in four countries concluded that a combination of vertically structured centralized and community-based approaches should provide short-term success as well as long-term sustainability.[173] Considerable importance is placed on negotiating behaviour and social change as opposed to education for knowledge change; resources and decision-making are decentralized; targeted government and private sector advocacy is deployed to increase political and financial commitment; extensive partnerships and support networks are developed through intensive mobilization; and greater focus is given to environmental improvements such as through better urban planning and services, including refuse disposal and water supply management, with the active involvement of communities.[174]

Apart from individual/family/community behaviour change, an "enabling" environment, i.e. one that supports, for example, new appropriate behaviours – perhaps by providing improved services, better housing/infrastructure construction techniques or superior policies and more effective legislation – is also imperative.[175]

Communication for behavioural impact (COMBI), espoused by WHO, is an innovative approach that refers to "…the task of mobilizing all societal and personal influences on an individual and family to (ensure) prompt individual and family action."[at] COMBI focuses on and is informed by behavioural outcomes that are made explicit, while health education and promotion may be dedicated to behavioural outcomes stated implicitly.[au]

COMBI's premise is that while knowledge of effective tools and technologies, availability of services, etc. needs to be introduced or reinforced, that alone is not enough, since knowing what to do is in reality different from doing or adopting appropriate activities without the necessary motivation and an enabling environment. In other words, an informed and educated individual is not necessarily a behaviourally responsive one. COMBI's process blends strategically a variety of communication interventions intended to engage individuals and families in considering recommended healthy behaviours and to encourage the adoption and maintenance of those behaviours.[av]

COMBI thus entails purposive and tailor-made strategic communication solutions intended to engage a specific target audience to translate information into responsive action and integrate it with advocacy and social mobilization initiatives to create an enabling environment. Such an environment will result in desired behavioural outcomes and impact.

Developed and tested over several years, COMBI incorporates the lessons learnt from five decades of public health communication and draws substantially from the experience of private sector consumer communication.[176] In effect, COMBI represents a neat coalescence of a variety of marketing, communication, education, promotion, advocacy and mobilization approaches that

as Changes that are frequently resisted have been described in chapter 12.
at World Health Organization, Mobilizing for Action: Communication-for-Behavioural-Impact (COMBI). 2004. WHO. *http://www.k4health.org/sites/default/files/COMBI.pdf*
au *http://www.comminit.com/pdf/Combi4-pager_Nov_14.pdf*
av ibid.

generally aim to do the same thing: have an impact on behaviour and foster programme–community partnerships by integrating principles and techniques of health education and promotion.

Furthermore, "it is almost an article of faith that locating programmes in the community and involving community members in planning, implementation and evaluation can be an effective strategy for improving population health".[177] Using participatory methods to include people in the designing, implementation and evaluation can be a productive way to start understanding the motivational gaps and barriers[aw] and ensuring sustainability, which are integral to COMBI planning and implementation as well. New evidence-based methodologies focus on furnishing community members with key concepts and evidence-based training so that they gather their own data, evaluate the control programme and generate and implement their own improved interventions based on the successes and challenges encountered in their settings.

11.1 Planning social mobilization and communication: A step-by-step guide

The step-by-step guide on planning social mobilization and communication for dengue fever prevention and control using the COMBI approach by the World Health Organization (2004) provides clear guidance on designing national communication and social mobilization plans and its implementation and monitoring and evaluation.[178] COMBI planning comprises 15 steps (*Box 30*):

Box 30: Fifteen steps of COMBI planning

(1) Assemble a multidisciplinary planning team.
(2) State preliminary behavioural objectives.
(3) Plan and conduct formative research.
(4) Invite feedback on formative research.
(5) Analyse, prioritize, and finalize behavioural objectives.
(6) Segment target groups.
(7) Develop strategy.
(8) Pre-test behaviours, messages and materials.
(9) Establish a monitoring system.
(10) Strengthen staff skills.
(11) Set up a system to manage and share information.
(12) Structure the programme.
(13) Write a Strategic Implementation Plan.
(14) Determine budget.
(15) Conduct a pilot test and revise the Strategic Implementation Plan.

aw A classification derived by a literature review by Mefalopulos (2003) includes (1) passive participation, when stakeholders attend meetings to be informed; (2) participation by consultation, when stakeholders are consulted but the decision-making rests in the hands of the experts; (3) functional participation, when stakeholders are allowed to have some input, although not necessarily from the beginning of the process and not in equal partnership; and (4) empowered participation, when relevant stakeholders take part throughout the whole cycle of the development initiative and have an equal influence on the decision-making process. Cited from: Mefalopulos, P. Development Communication Source Book: Broadening the boundaries of communication. 2008. World Bank. *http://siteresources.worldbank.org/EXTDEVCOMMENG/Resources/DevelopmentCommSourcebook.pdf*

Each organization's planning/processes include different names for the steps but there are common elements. Most key steps should engage the participation of members of the intended audience and other key stakeholders.[ax]

Following the 15 steps of COMBI planning, starting with establishing clear behavioural objectives (and not just knowledge change), the strategic roles of a variety of social mobilization and communication actions (*Box 31*) and their integrated application as suitable is determined.[ay]

Box 31: COMBI's integrated actions

(1) **Public relations/advocacy/administrative mobilization:** to place the particular healthy behaviour on the agenda of the business sector and administrative/programme management via the mass media (news coverage, talk shows, soap operas, celebrity spokespersons and discussion programmes); meetings/discussions with various categories of government and community leadership, service providers, administrators and business managers; official memoranda; and partnership meetings.

(2) **Community mobilization:** including the use of participatory research, group meetings, partnership sessions, school activities, traditional media, music, song and dance, road shows, community drama, leaflets, posters, pamphlets, videos and home visits.

(3) **Sustained appropriate advertising:** in M-RIP (massive, repetitive, intense and persistent) mode via the radio, television, newspapers and other locally available media, to engage people in reviewing the merits of the recommended behaviour vis-à-vis the "cost" of carrying it out.

(4) **Personal selling/interpersonal communication/counselling:** involving volunteers, schoolchildren, social development workers and other field staff at the community level, in homes and particularly at service points, with appropriate information and literature and additional incentives, and allowing for careful listening to people's concerns and addressing them.

(5) **Point-of-service promotion:** emphasizing easily accessible and readily available vector control measures and fever treatment and diagnosis.

Fifteen steps of COMBI planning

Step 1: Assemble a multidisciplinary planning team

Dengue fever epidemiology is complex and requires a mixture of expertise in different disciplines to define the set of technically sound solutions. Team members might include physicians, epidemiologists, entomologists, social scientists, health communication specialists, community development workers, urban planners, water/civil engineers and advertising/media experts. Social scientists/communication specialists are the key persons to understand the demands of control of dengue vectors (example,

ax Johns Hopkins Bloomberg School of Public Health. Center for Communication Programs. Knowledge for Health Project, The Tools for Behaviour Change Communication. January 2008 • Issue No. 16. *http://info.k4health.org/inforeports/BCCtools/BCCTools.pdf*

ay For additional information, refer to the Parks W., Lloyd L.. Planning social mobilization and communication for dengue fever prevention and control: A step-by-step guide. WHO, Geneva 2004 (WHO/CDS/WMC/2004.2 and TDR/STR/SEB/DEN/04.1). Additional literature include: 1) SEPA (Socializing Evidence for Participatory Action) programme based on CIET methods *(http://www.ciet.org/en/);* 2) Parks W. et al., International Experiences in Social Mobilization and Communication for Dengue Prevention and Control. Dengue Bulletin 2004; 28 (Supplement): 1–7; 3) Mefalopulos, P.. Development communication source book: Broadening the boundaries of communication. 2008. World Bank. *http://siteresources.worldbank.org/EXTDEVCOMMENG/Resources/DevelopmentCommSourcebook.pdf;* 4) Carbanero-Versoza, C.. Strategic communication for development projects: A toolkit for task team leaders. 2003. World Bank. *http://siteresources.worldbank.org/EXTDEVCOMMENG/Resources/toolkitwebjan2004.pdf*

through IVM) on the one hand and the diversity of cultures, literacy and degree of poverty of urban and rural populations on the other hand to evolve suitable strategies.

The terms of reference should include the following:

- Determining preliminary behavioural objectives *(see Step 2)*.
- Recruiting principal investigators and field workers (as required) to design and conduct formative research *(see Step 3)*.
- Organizing feedback on the formative research findings *(see Step 4)*.
- Finalizing behavioural objectives *(see Step 5)* on the basis of research findings.
- Designing the strategy *(see Steps 6 and 7)*.
- Overseeing pre-testing of messages, materials and behaviours *(see Step 8)*.
- Ensuring that monitoring and evaluation activities are conducted and relevant reports written *(see Steps 9 and 11)*.
- Supervising/participating in relevant training activities *(see Step 10)*.
- Writing a Strategic Implementation Plan that details the social mobilization and communication strategies required to achieve the stated behavioural objectives *(see Step 13)*.
- Seeking financial and other support in kind for the proposed project/activity *(see Step 14)*.
- Identifying the location of a pilot project and discussing subsequent design and implementation with the relevant community and civic authorities *(see Step 15)*.
- Presenting the programme progress to community groups, relevant national committees, donor agencies and the national media, as required.
- Presenting programme results at relevant forums (meetings, symposiums, etc.).

Step 2: State preliminary behavioural objectives

Achievement of specific behavioural results vis-à-vis behavioural objects is the essence of COMBI planning. Hence, at the very start enunciation of preliminary behavioural objectives is absolutely imperative.

In developing the preliminary objectives, the planning team must discuss the following questions:[az]

- Whose behaviour should be changed to bring about the desired outcomes? Who is the target audience?
- What is required to be done? Is it feasible? Is it effective?
- Why are they not doing it now? What are the barriers and motivators?
- What activities can address the factors most influential to change behaviour?
- Are materials/products/services needed to support those activities? If yes, are those easily available? If not, what should be done?

az Drawn from: Parks, W. and Lloyd L.. Planning social mobilization and communication for dengue fever prevention and control: A step-by-step guide. WHO. 2004.[178]

Step 3: Plan and conduct formative research

Formative research (also known as market or intervention or communication research) is conducted primarily at the start of the programme and includes all research that helps to inform the development of a new, or refinement of an existing, social mobilization and communication strategy.

The key focus areas of research are described in *Box 32*.

Box 32: Formative research

Formative research:

- Identifies key socioeconomic issues, gaps in knowledge and health education, and key resource- and non-resource-related constraints that impede existing prevention or control programmes.
- Provides in-depth information about attitudes, beliefs and practices about health and the factors affecting health behaviours among the target audience and ascertains the degree of access to information, services and other resources.
- Highlights the felt needs in the community that could be shared by programme priorities.
- Keeps those developing the strategies informed about what local populations are doing, thinking, and saying about focal issues, behaviours, technologies and service staff.
- Discovers key cultural analogies that can be used for effective health education messages and materials.
- Identifies behaviours that, after modification, could become more effective in removing or reducing health risks; and examines what obstacles may come in the way of adopting new behaviours and how to resolve them.
- Investigates barriers, motivations and opportunities for change and identifies the stage people are at in the behaviour change process.
- Points out the degree of access to information, services and other resources, and basic media habits.
- Examines recent and current programmes and policies, assesses structures, scope and capabilities of programme planners and implementers, and provides details on how best to implement the strategy (who, when, where, how).
- Records the availability of communication channels and their strengths and weaknesses in terms of reaching the target audience.
- Pre-tests behaviours, messages, and materials with representative samples of intended target groups.
- Assesses health workers' and/or policy-makers' perceptions and practices.
- Lists the stakeholders and partners for planning, implementation and monitoring of COMBI programmes and the motivations, skills and resources required to ensure their active involvement to make dengue prevention and control everyone's business.
- Monitors community response to interventions over time, enabling mid-course correction.

A specific body of research in addition to a series of practices to induce change through specific methods and media is essential in development communication. While there is vast literature about planning, production and strategic use of media in development, there is significantly less material

about the "dialogic" communication to investigate issues at the beginning of development projects and programmes.

It is well recognized that communication is a horizontal process aimed, first of all, at building trust, then assessing risks, exploring opportunities, and finally facilitating the sharing of knowledge, experiences and perceptions among stakeholders. The aim of this process is to probe each situation through communication in order to reduce or eliminate risks and misunderstandings that could negatively affect project design and success. Only after this exploratory and participatory research has been carried out does communication regain its well-known role of communication of information to specific groups and trying to influence voluntary change among stakeholders.[ba]

For carrying out research, research design and protocol must be developed at the outset. Emphasis should be on qualitative research while quantitative information should also be gathered. In-depth interviews, focused group discussions, and observations, etc. should be considered. Institutional capabilities must be assessed to carry out research and identify who will conduct it.

Selection and contracting should be executed as necessary. Questionnaire/interviewer guides must be developed, pre-tested and revised and a field plan for the research (responsibilities, schedules, etc.) should be prepared. Research staff (from the contracted organization) must be trained and conducted to facilitate/support research. Information should be carefully collated and analysed and a final formative research report with findings and implications for programme activities prepared. The key steps are presented in *Box 33*.

Box 33: Key steps for conducting a formative research

The following steps provide an idea of what to schedule for. Time estimates given are for a full study investigating all issues rather than for a specialized study:

(1) planning the research (4 weeks).
(2) training (3 weeks).
(3) field work (6 weeks).
(4) analysis and writing summary report of findings (6 weeks).
(5) final report writing (3 weeks).
(6) dissemination.

The cost of the research will vary depending mainly on how many communities need to be visited (sampled) and the cost incurred on personnel and transport. The larger the geographical area and the more diverse the population, the greater the number of days required in the field and more expensive the research.

Engagement of target audience/community/group/individual: Sensitize and discuss the objectives and purpose with the target. Select participants who work with or represent those most affected by the health issue and ensure fair representation of vulnerable segments such as women and marginalized groups. Encourage response regarding their felt needs and involve them and other key stakeholders in analysis of concerns. Various participatory methods should be employed. These may include preference ranking, scoring of various problems and solutions (for example, programme interventions for vector control) in addition to mapping the availability of various programmes and prioritizing the best mode/place for implementation.

ba Mefalopulos, P.. Development communication source book: Broadening the boundaries of communication. 2008. World Bank. *http://siteresources.worldbank.org/EXTDEVCOMMENG/Resources/DevelopmentCommSourcebook.pdf*

Step 4: Invite feedback on formative research

On the basis of formative research, the planners and decision-makers should make suitable recommendations for action by different segments of the programme.

Step 5: Analyse, prioritize and finalize behavioural objectives

- Examine critically.
- Alterations of the objectives originally set should respond to the outcome of formative research.
- Target a few behaviour items.
- Choose not more than three behavioural objectives at a time.

COMBI objectives are different from the objectives to which one is used to because it includes:

- the clear identification of the target audience (e.g. "housewives who store water" rather than "households").
- a detailed description of the behaviour being promoted and the frequency of the behaviour (e.g. "scrub the interior walls of water-storage drums twice a week with a rigid bristle brush and laundry detergent" rather than "scrub water-storage containers to prevent mosquito production").
- the measurable impact that is desired over a specific time period (e.g. "60% of women who store water will scrub the interior walls of … after the first year of the programme" rather than "all women will scrub water-storage drums").

In other words the objectives should be 'SMART' (specific, measurable, appropriate, realistic, time-bound).

- *Specific:* who or what is the focus; what change(s) are intended.
- *Measurable:* specified quantum (e.g. % change intended).
- *Appropriate:* based on target needs and aimed at specific health-related benefits.
- *Realistic:* can be reasonably achieved.
- *Time-bound:* specific time period to realize the objectives.

Step 6: Segment target groups

In view of the diversity of the thinking processes of the community, perceptions about a particular message may differ. In contrast, if the messages are segment-specific, it is then seen as concerning that segment alone.

There are two main advantages to segmentation:

- Meeting the needs of the smaller segments is better than targeting everyone.
- Since operation is often attempted with very limited resources, one can become more efficient and effective if it is determined as to which segments demand more resources than others and strategies are tailored accordingly.

Step 7: Develop strategy

A "strategy" is the broad approach that the programme takes to achieve its behavioural objectives. Strategies are made up of specific social mobilization and communication activities that on their

own or in combination lead to the achievement of the objectives. *Box 34* gives an example of how objectives, strategies and activities may be linked.

Box 34: Objectives, strategies, activities

Objective

To prompt 1000 householders in [location] to prevent any tyre that is not in use for a car from accumulating water during the next 12 months.

Strategy

(one of several, each aimed at different target groups).

To drill holes in discarded tyres to stop them from collecting water. The strategy will be delivered in two ways:

- A field team of 30 volunteers and five vector control programme staff will visit households and drill holes into tyres with hand-held battery-driven drills.
- Tyre replacement centres and gas stations and the like will provide an ongoing drilling service when old tyres are exchanged for new ones but are still wanted by householders, and before storing unwanted tyres at a public dump site.

Activities

- Training workshop for field team on communication skills and the drilling of old tyres.
- Field team to visit 1000 households and drill holes in old tyres as well as disseminate information on vector control.
- Interpersonal communication (IPC) with householders supported by information dissemination pamphlets.
- Pamphlets handed out to drivers by sales staff and cashiers at tyre replacement centres and gas stations.
- Radio and TV spots to raise awareness about the mosquito breeding problem in used/dumped tyres and drilling those for channelling out water.
- Letters and follow-up telephone calls and visits to tyre replacement centres and gas stations.

Strategy development requires creativity. Frequently, it is not the lack of funds, knowledge, technology, skilled employees, or motivated communities that is the principal impediment; **what programmes lack most is a supply of new ideas**. No effective dengue control programme can exist without an innovative approach to social mobilization and communication because everything must change on a regular basis. An example of creativity at work is illustrated in *Box 35*.

Box 35: Dengue Bicycle-Riders in Johor Bahru, Malaysia[178]

As part of a carefully integrated social mobilization and communication campaign in Johor Bahru in Malaysia, bicycle-riding teams (D'RIDERS) were formed to undertake tours of the district every Sunday during the three-month campaign. These riders were local youths who volunteered for this activity. Each team consisted of 20 riders.

Every Sunday morning, the team toured selected areas on bicycles accompanied by a van equipped with a public announcement system to promote the campaign. They rode on mountain-terrain bikes clad in special T-shirts with the two behavioural objectives of the campaign printed on the back ("Every family should carry out a house inspection once a week for 30 minutes" and "Anyone with fever should seek immediate treatment in a clinic").

At each location, the team was greeted by local community leaders and residents and the atmosphere was "carnival-like". There were speeches delivered, along with distribution of health education materials, refuse-collection activities, traditional dances and singing, and occasionally some competitions. Refreshments were also served.

Designing strategies depends on the objectives to be achieved and the resources available. A number of resources are necessary to ensure four important design features of good strategies: consideration given to more than just the "message"; the careful blending of communication actions; gender sensitivity; and the timing of interventions to coincide with local events and calendars.

Effective communication is central to achieving behavioural outcomes and impact. Communication is the process in which a **M**essage from a **S**ource is sent via a **C**hannel to a **R**eceiver with a certain **E**ffect intended with opportunities for **F**eedback, all taking place in a particular **S**etting (MS.CREFS)[bb] [Table 13].

Table 13: MS.CREFS components

Components	Important considerations
Message	Ensure that the language is *clear and easily understandable*. That it is not too technical. Giving too many messages confuses the audience. Be clear about what is the main central message.
Source	*Use a credible person to deliver the message*. For example, people may not pay attention if a local shopkeeper was giving advice about dengue, but it would be more credible if a well-known doctor was delivering the same. In other cases, a young teenager would be more likely to persuade other teenagers to take action rather than a figure seen as authoritarian. Remember, appearances make a difference in how the source is perceived.
Channel	Identifying the most appropriate channel is important, either using the mass media through radio, television and newspaper and/or interpersonal channels such as door-to-door visits, traditional theatre, group meetings, etc. The *right channel must be used for the right target audience and generally the most effective is a selective mix of channels*. Note the importance of non-verbal channels such as gesticulation, facial expressions and posture.

bb ©Everold Hosein

Components	Important considerations
Receiver	*The receiver filters and interprets the world through the cultural lens* with which they view the world. An understanding of this world is crucial to effective communication. Therefore, how you would explain the need to correctly protect water containers to a rural farmer may be different from how one would deal with urban schoolchildren and housewives.
Effect	This is the end result of communication. The effect is the behavioural focus through *improving knowledge, skills and providing prompts/triggers that could have an impact on ultimate behavioural outcomes*. This is the point of departure for COMBI planning. One must be clear about the communication effect(s) desired that would lead to behavioural results.
Feedback	It is important to ensure that *communication interventions are appropriate, effective and engage the receiver to provide feedback*. Feedback allows for such assurance. With it one can fine-tune communication actions.
Setting	*This can facilitate or hinder communication*. If there is too much noise, or the timing is wrong, or the setting is inappropriate to the subject being discussed, or there are too many distractions, or it is too hot, or too cold, all these factors affect how messages are heard and interpreted. Locations such as religious venues, health centres, cafes, marketplaces and schools provide their unique features that can affect the dynamics of communication and must be considered in the planning of communication actions.

Source: Parks W., Lloyd L.. Planning social mobilization and communication for dengue fever prevention and control: A step-by-step guide. WHO, Geneva 2004 (WHO/CDS/WMC/2004.2 and TDR/STR/SEB/DEN/04.1)[178]

Engagement of the target audience/community/group/individual: Involve targets, stakeholders and/or facilitate their involvement in strategy design consultations or workshops that should include deliberations on MS.CREFS . Such events should be held at locations preferred by the community and at times that are convenient for them. The workshops should arrive at a consensus regarding strategic planning. The stakeholders should "buy in" by agreeing to take on responsibilities as appropriate.

Step 8: Pre-test behaviours, messages and materials

Pre-testing is the hallmark of a well-designed social mobilization and communication strategy. The study should be designed and carried out by social scientists. The subject matter for pre-testing includes: (i) product testing, (ii) behavioural trials, and (iii) message and material testing.

(i) ***Product testing*** helps avoid what could be called the "product mindset". In this mindset, it is presumed that if any Aedes breeding control measure (example, e.g. larvicide, water container cover) is offered to the community it will be accepted/followed/used. However, in the absence of visibility, i.e. if dengue is not perceived to be a problem or if dengue cases occur despite vector control or if people continue to be bitten by mosquitoes despite Aedes control or if mosquito breeding is thought to be in areas such as swamps and drains (not in cleaner household water containers), or use of certain measures is thought to contaminate water supplies, Aedes control measures often have no clear advantage for the communities, in general. So, decision-makers have to generate evidence for the acceptance of the product.

(ii) ***Behavioural trial*** is a small-scale test of a new behaviour with a representative sample of the target group to determine its abilities to effectively adopt a different practice (sometimes, behavioural trials and product tests are combined). A behavioural trial can help to:

- analyse those parts of the desired behaviour that are, and are not, readily adopted;
- identify material or behavioural barriers to the adoption of the new behaviour;
- identify what works best to reinforce learning of the new behaviour; and
- refine communication to reinforce the desired behaviour.

(iii) ***Pre-testing messages and materials*** including brochures, booklets, flipbooks, information cards, scripts for plays/skits/story boards as relevant for entertainment education/infotainment (information through entertainment), print, radio or TV advertisements, audiotapes or videotapes, packaging of technical products, etc. These help to:

- assess whether messages are clear and compelling;
- identify unintended messages;
- detect totally unpredictable audience responses and other aspects of materials that may require modification;
- select from among a range of potential messages and materials and provide some insight into whether these messages and materials will generate the desired behavioural impact.

Effective messages should be clearly stated and specific to the desired action(s)/behaviour(s), technically correct, consistently repeated, easy to understand, command attention; and should appeal to both the heart and the head, build trust and call for action.

Engagement of the target audience/community/group/individual: Form a group of key stakeholders close to or representing the audience. Advisory groups can provide useful advice about developing appropriate messages and materials and can help with suggesting revisions after pre-testing. Invite members of the audience to suggest messages and materials.

Step 9: Establish a monitoring system

Monitoring of any programme is continuous and enables the desired modification of the strategy to achieve the desired goals. Evaluation is either periodic or a terminal activity. Monitoring and evaluation (M&E) demonstrate if a particular intervention/medium has reached/served its goal/purpose or not. M&E also helps obtain guidance for programme decisions and determine if improvements in health outcomes are causally linked to a given intervention or a given behavioural change.[bc]

There are two ways to monitor strategy progress:

(i) Behavioural impact monitoring (or surveillance), and

(ii) Process evaluation.

(i) ***Behavioural impact monitoring:***

Individual behaviour change will be reflected by an increase or decrease in (i) production of adults of *Ae. aegypti* mosquitoes; (ii) the risk of other members of the family being bitten by *Aedes* mosquitoes; and (iii) the risk of acquiring dengue virus infection.

(ii) ***Process evaluation:***

Process evaluation will help in utilization of the data in three ways:

- Making decisions about refining the strategy's objectives, activities, behaviours, products, services and so on.
- Documenting and justifying how resources have been spent.
- Making a compelling case for continued or additional funding (especially if combined with behavioural impact data).

bc For additional information, refer to: Tools for Behaviour Change Communication. INFO project. Center for Communication Programs. Johns Hopkins Bloomberg School of Public Health. 2008. Issue No. 8. *http://info.k4health.org/inforeports/BCCtools/BCCTools.pdf*

Process evaluation may be carried out by way of tracking planned activities, field supervision and monitoring by using the standardized supervision checklist. Regular supervision ensures that any gap or problem with knowledge, skills or attitude is readily recognized and corrected.

Mid-term and end-term evaluations, as appropriate, should be planned and conducted. These should be a component of the overall programme evaluations or may be conducted independently, as necessary and appropriate. The information generated through formative research should serve as the baseline. Both quantitative and qualitative methods should be applied.

Engagement of the target audience/community/group/individual: Comparison of outputs, outcomes with shared vision and original objectives is important. For purposes of continued motivation and reward, it is important that most of the community/stakeholders participate in the M&E process so that lessons learnt about what worked and why are shared and the way forward discussed. Include the target audience and other stakeholders (as part of steering committees, etc.) to track the progress of implementation, make recommendations and ensure action to improve activities. Involve the target audience in evaluating the programme(s) against the parameters they set themselves (participatory evaluation). Discuss their involvement in conducting the evaluation, and how the results will be used. Encourage the sharing of evaluation findings within the community and with others, as well as advocate further activities.

In 2005, an evaluation of 11 WHO-supported dengue communication and mobilization programmes using the COMBI planning tool was conducted in six South Asian and Latin American and Caribbean countries.[179] Certain key issues from the conclusions derived from this evaluation, as well as from the review of recent programmes,[bd] are presented in *Box 36*.

Box 36: Key Issues from COMBI evaluation from South Asian and Latin American and Caribbean countries

Key issues:

- Programme leadership and planning for sustainable community participation and involvement.
- Transfer of technical knowledge and skills in planning participatory behavioural interventions to health workers, community volunteers and other partners at the local level.
- Creation and maintenance of monitoring and feedback systems at the local and national levels, including the development of behavioural indicators.
- Judicious mix of communication channels (interpersonal, mass media, publicity, etc.) to support programme behavioural goals over time, based not just on available funding but also on effectiveness in the local context.

Step 10: Strengthen staff skills

Long-term sustainability of social mobilization and communication will be difficult unless the organization and orientation of government-run services emphasizes the development of community-based programmes with genuine decision-making at the local level. Where programmes have undergone decentralization or are currently being decentralized, capacity at provincial, district and

bd Achieving Behaviour Change For Dengue Control: Methods, Scaling Up and Sustainability Working Paper for the Scientific Working Group, Report on Dengue, 1–5 October 2006, Geneva, Switzerland, World Health Organization on behalf of the Special Programme for Research and Training in Tropical Diseases, 2007. *http://www.who.int/tdr/publications/publications/swg_dengue_2.htm*

sub-district levels to plan, manage and implement social mobilization and communication strategies is often far from sufficient. It is, therefore, essential to provide opportunities for service personnel/ volunteers involved in the programme to learn how to plan and implement appropriate social mobilization and communication strategies, how to listen and work with community members, and how to link their plans and activities with local perceptions, conditions and resources.

Training programmes should have feedback, and pre- and post-test sessions in addition to brainstorming on the major challenges in planning and implementing social mobilization and communication programmes for malaria. Further, group work should be organized on various prevention and control components with the exercises focusing on related current behaviours, desired behaviours, target audience, communication, objectives, key benefits, key barriers, draft messages, interventions, monitoring and evaluation, etc., thereby ensuring that skills are developed or refreshed. These should draw from the experiences of trainees/trainers.

Step 11: Set up systems to manage and share information

Programmes can no longer rely on their former practices to sustain dengue prevention and control. The ability to change requires an ability to learn. Dengue programmes need to become "learning organizations", with information management systems that enable rapid understanding of trends and developments affecting the behaviour of target groups. Such systems would include carefully filed or electronically stored data on target groups and programme partners, drawing from formative research (see Step 3) as well as from pre-testing (see Step 8), monitoring (see Step 9), and negotiations with programme partners (see Step 12). This information system may be called "Community Profiles" or "Consumer Information System" or the "Formative Research Databank". In essence, a COMBI database is needed as equivalent to a health information system or entomological surveillance system.

Such database and archived research findings and lessons learned should be used in future programmes and/or for revising/redesigning communication, behaviour change objectives, channels, messages, tools, materials, indicators, etc. and for restarting the strategic designing/planning, till the desired behavioural objectives are achieved.

The programmes should plan and prepare information products for dissemination among key stakeholders, partners, news media, funding agencies and the like.

Step 12: Structure of the programme

Social mobilization and communication are usually accorded low priority in most programmes and are often developed and implemented at the lowest levels (by junior staff or staff with no relevant background/experience). The obvious implication of this structural location is that senior management doesn't consider it to be very important. Organizational or structural change is often required.

Strategies for organizational change may include:

- forming multidisciplinary teams and intersectoral committees to help managers work through the tasks required;
- training, mobilizing and supervising a field workforce;
- establishing management procedures, benchmarks (indicators that show whether the programme is moving towards a particular goal), and feedback or tracking mechanisms (e.g. monthly reports or newsletters shared at all levels and regular meetings); and
- designing a modified organizational structure by identifying and delineating new responsibilities, creating new positions (when necessary), modifying working hours, and covering the expenses that increased field work generates.

Four basic organizational structures (not mutually exclusive) can be used to enable programmes to practise social mobilization and communication. They are:

- Functional organization (namely involving a number of staff and consultants, and the creation of working groups).
- Programme-centred organization (namely an identified staff given the responsibility of coordinating all functions).
- Community-centred organization (namely structuring the programme in accordance with how the interventions are perceived by community groups, i.e. on the basis of how they use them and what they think about them, and not on how the programme promotes them).
- Organizing strategic alliances (namely involving partner organizations such as NGOs, other ministries, advertising agencies, etc.).

Step 13: Write a strategic implementation plan

The purpose of strategic planning for social mobilization and communication is to devise a plan that is appropriate to the health problem and target audience, takes into account the resources available, and has the best chance of bringing about sustainable behavioural impact. It should be locale- and context-specific and ensure implementation in a socioculturally and economically appropriate way.

Plans[be] can be short-term and long-term. While 'short-term' normally refers to a period of one year or less, "long-term" plans usually extend to three to five years.

The plan should focus on enhancing awareness among the targeted at-risk and affected groups about source and transmission risk reduction, treatment and availability of services. It should also address and promote attitudinal and value changes among target groups that would lead to informed decision-making and modified behaviour (such as the adoption of timely and appropriate practices at the individual, family and community levels), and stimulate an increased and sustained demand for quality prevention and care services and optimal utilization of available services. The plan should be discussed and debated by the multidisciplinary planning team and by other stakeholders. Ideally, there should be three basic sections, as enunciated in *Box 37*.

Box 37: Basic sections of a strategic implementation plan[178]

1. INTRODUCTION

1.1 Principal findings from formative research: Prepare a summary of existing data and results of the formative research on the behavioural and programme environments, including a list of issues requiring further formative research.

1.2 Behavioural analysis: Write down a detailed description of the behaviours selected for attention through the analysis process (for example, problem analysis, risk factor analysis, force-field analysis, BEHAVE framework analysis, priority analysis, SMART objective analysis). State the behavioural objective(s) [ensure that the objectives are SMART: specific, measurable, appropriate, realistic and time-bound]. Explain the significance of the objective/s.

1.3 Target group segmentation: Describe target groups (classified by behavioural segments and primary and secondary audiences).

be Also referred to as 'Action' or 'Operational Plan'

2. THE STRATEGIC APPROACH (explaining the "what", "why" and "how")

2.1 Overall goal: Define the overall goal, for example: "to contribute to the reduction in morbidity and mortality from dengue fever/dengue haemorrhagic fever in [location] by the year [date].

2.2 Behavioural objective(s): Define the behavioural objective(s). Re-state the specific objective/s as presented in 1.2. For example: *"Within one year from the start of the programme, to increase the percentage, from 30% to 60%, of women in [place name] who vigorously scrub the interior walls of water-storage drums twice a week using a rigid bristle brush and laundry detergent."*

2.3 Strategy(ies): A general overview of the social mobilization and communication strategy stating the key messages, their sequencing (if any), the overall tone of the strategy, the blend of communication actions (administrative mobilization, community mobilization, advertising, personal selling, point-of-service), and the relationships between different communication actions and an overview of how the plan will be managed. The strategy should focus on delivering the "right messages" to the "right audience" at the "right time" through the "right channel mix".

3. THE IMPLEMENTATION PLAN (explaining the "what", "when", "where", "who", "how much")

3.1 Communication actions: Detail specifications of communication actions outlined in the "Strategy" section, including descriptions and plans for production, procurement, pricing and distribution of any technological products, services, incentives (such as bags, caps, T-shirts, prizes) and other materials, as well as identifying what training and supervision activities are required for staff and/or partner agencies (for whom, what, when, where, why, and facilitated by whom). Drawing from the formative research, a locale- and context-specific media mix should be considered. Reach, credibility and costs should be discussed.

3.2 Monitoring and evaluation: Determine the details of the behavioural monitoring and process evaluation to be used, outline the methods for data collection and analysis, prepare a description of the system for managing and sharing monitoring information (community feedback, programme reports, etc.), and ready an explanation of how the plan will be modified as a result of monitoring. Also included here would be a description of any mid-term or final evaluations of behavioural impact (alongside other areas of interest such as entomological impact, social and organizational impact, impact on morbidity and mortality, environmental impact, cost–benefit analyses, and other unintended impacts).

3.3 Management: Describe the management team (e.g. the multidisciplinary planning team), including specific staff or collaborating agencies (e.g. local advertising firms and research institutions), designated to coordinate communication actions and other activities (such as monitoring). Also consider including any technical advisory group or government body from which the management team is to receive technical support or to which it will report.

3.4 Workplan: Develop a detailed workplan with time schedules for the preparation and implementation of activities required to execute each communication action as described in Section 3.1. The workplan could take the form of a table with column headings such as 'Activities', 'Completion date', 'Responsibility' (staff member, partner agency, and so on), etc.. A tabular flowchart (or Gantt Chart) with column headings for weeks, months, quarters or years along the top and specific activities being listed as row headings down the left-hand side is also useful. Cells within the table can be shaded to indicate the week or month during which a particular activity is scheduled.

Such a diagram allows instant comprehension of when different activities begin and end, whether preparatory activities have been given enough time, whether communication actions that need to be integrated have indeed been integrated, and highlights periods of peak activity.

3.5 Budget: Work out a detailed list of costs for the various activities (*see Step 14*).

Engagement of target audience/community/group/individual: Ensure that discussions are held with the target audience prior to finalization of the plan and encourage them to understand various roles and responsibilities in programme implementation and share their views on participation and self-monitoring.

Step 14: Determine the budget

Dengue is basically a problem of domestic and workplace water management and sanitation, and the behaviours required to improve this management are considerably cheaper than largescale application of insecticide. But it would be a mistake to believe that the problem can be addressed with little or no investment of funds and commitment of other resources (e.g. staff and time). It is a **huge challenge** to find ways of transferring to the community the desired degree of responsibility, capability and sense of motivation for the prevention and control of dengue. An appropriate budget should be allocated for these important activities.

Step 15: Conduct a pilot test and revise the strategic implementation plan

While a lot of attention needs to be devoted to the objectives, strategies, activities and monitoring procedures of the strategic implementation plan, and the resources needed for its implementation, the "process" of social mobilization and communication implementation is often overlooked. Pilot-testing represents an important first step in implementing a social mobilization and communication plan. During piloting, formative research is again used to obtain feedback from participants involved in the plan's implementation as well as from the staff on the quality of the activities covering all dimensions from educational materials to the competence of the personnel chosen to deliver the activities.

Pilot-testing serves at least three basic functions:

- Ensuring that the chosen strategies have no obvious major deficiencies.
- Fine-tuning possible approaches so that they speak to target audiences in the most effective ways.
- Convincing staff and partners.

No matter how the behavioural results from the pilot test are captured, stored or analysed, the next important task is to determine whether the strategy can proceed to full implementation or whether modifications are needed. Here, the community-centred view of planning must dominate.

In other words, the focus of learning should be on what primary and secondary audience members said, what they did, what additional information and resources they wanted and in what form, and so on. A pilot-test may reveal the need for re-setting the behavioual objectives, as well as redesigning strategy and approaches and also the plan of implementation itself.

Engagement of target audience/community/group/individual: Mobilize the target audience and other stakeholders in the pilot-test while including a control group/community among whom nothing beyond routine activities have been conducted.

The above-mentioned 15 steps of COMBI planning will accomplish three essential managerial tasks:

- *First, to establish clear behavioural objectives.*
- *Second, to determine the strategic roles of a variety of social mobilization and communication disciplines; for example, public relations, advocacy, administrative mobilization, community mobilization, advertising, interpersonal communication, and point-of-service promotion, in achieving and sustaining these objectives.*
- *And third, to combine these disciplines into a comprehensive plan that provides clarity, consistency and maximum behavioural impact to the social mobilization and communication efforts.*

The overall process or cycle of development communication, as in COMBI, too illustrates four main phases: research, is the first phase communication-based assessment (CBA) for obtaining inputs for strategy design, makes up the second phase. The next phase concerns the production of the materials and implementation of the planned activities. Finally, the fourth phase is concerned with evaluation. Proper evaluation of the impact of the communication intervention requires the definition of monitoring and evaluation indicators during the initial research phase.[bf]

It is well acknowledged that social mobilization and communication is an ongoing process, which is mostly non-linear and cyclical. Examples of non-linear models have been developed and applied across the world.[bg] Sustainable behaviour change requires time and repeated effort. The results and lessons from evaluation are utilized for refinement of the strategy (Step 7). The other steps, namely, developing and pre-testing messages and materials, the strategic implementation plan, M&E, etc. continue till the desired behavioural objective/s is/are achieved.

11.2 Ensuring health-care infrastructure/service/goods provision

Many a time behaviour change at the individual/community level may be limited to a short duration in time unless other measures/programmes are undertaken to ensure that the changes are self-sustaining. Since most behaviour change interventions are delivered through the existing structure of dengue programmes, for the most part, after a certain period the programme reverts to its original focus and programming: that is, entomological surveying and source reduction conducted by vector control staff. This is not only the case for behavioural interventions, but laboratory and case management also tend to function independently even though the need to integrate the five essential components (epidemiology, entomology/vector control, community participation, laboratory and case management) has been highlighted over the past years.[180,181,182]

bf Mefalopulos, P. Development Communication Sourcebook: Broadening the boundaries of communication. 2008. World Bank. *http://siteresources.worldbank.org/EXTDEVCOMMENG/Resources/DevelopmentCommSourcebook.pdf*

bg P-Process by the Johns Hopkins Bloomberg School of Public Health/Center for Communication Programs *(http://www.hcpartnership.org/Publications/P-Process.pdf)*; Planning and Implementing a Communication Program by the World Bank *(http://siteresources.worldbank.org/EXTDEVCOMMENG/Resources/toolkitwebjan2004.pdf)*

11.3 Application of COMBI

Many countries have applied COMBI for dengue prevention and control. A few examples are presented in *Box 38* and *Box 39*.[bh]

Box 38: Application of COMBI in Colombia[184]

A dengue prevention initiative was applied in the city of Bucaramanga in northeastern Colombia. Use of qualitative and quantitative research, including formative research, and data analysis based on the "Stages of Change" model was the basis for planning an integrated social mobilization and communication approach. The model classifies individuals according to where they fall in the behaviour change process:

(i) pre-contemplation: the person is not thinking of changing his or her behaviour (21% of housewives were found to be in this stage);

(ii) contemplation: the person begins to think about the action (50% were found to be in this stage);

(iii) preparation: the person plans to change the behaviour;

(iv) action: the person implements the plan to change the behaviour (29% were found to be in this stage); and

(v) maintenance: the person continues to practise the new behaviour.

The initiative focused on one day a week (i.e. Thursday) when residents were to seek and destroy the sites where the *Aedes aegypti* mosquito might occur and breed. On this day, communication and educational actions were used to mobilize and motivate people. Following this approach, innovative printed communication materials were designed and disseminated. This resulted in a massive mobilization of students, housekeepers and other members of the public. Materials and a methodology of interpersonal communication were additionally produced that generated partnerships with the private sector and community groups. Another innovative feature included a mobile dengue exhibit with interactive educational games.

The evaluation found that 94% of the teachers and 96% of the students knew about the calendar and 88% of the teachers and 77% of the students used it. The impact on households of message broadcast on radio in 2002–2003 recorded a score of 27% associating Thursday as "Dengue Prevention Day" and the same percentage practising specific actions to look for and control *Ae. Aegypti* breeding sites on that day of the week. The number of houses and schools with immature *Ae. aegypti* was found to be fewer during the post-intervention evaluation compared with the pre-intervention survey. To monitor behavioural impact among housewives and the rest of the population, the House Index was measured every three months. The results showed the index had decreased from 18% in 1998 to 5% in 2003.

The three most important lessons learnt from this exercise included:

(i) Objectives should be based on results from research that combine appropriate qualitative and quantitative methods.

(ii) It is necessary to generate a critical mass of committed persons acting in different roles to prevent dengue.

(iii) In order to develop a behaviour change project, it is necessary to have at least three years of continuous work done before any significant changes are observed.

bh For additional examples, refer to *Dengue Bulletin 2004, Vol. 28* (Supplement).

Box 39: Application of COMBI in Sri Lanka[183]

Sri Lanka initiated COMBI for dengue prevention and control in 2009 in 12 high-risk districts on a campaign mode.

The overall goal has been to reduce the incidence of DF/DHF in the high-risk districts by 50% by the end of 2006 (i.e. from 2000 to 2005). The behaviour objectives for the period of 16 weeks from March and 12 weeks from September in select high-risk areas were to: 1) prompt housewives in 80%–90% of homes to remove breeding sites in their houses and surroundings every Sunday for 30 minutes; 2) motivate 80%–90% of tyre traders to keep their premises free of breeding sites; and 3) prompt school principals and teachers of 80%–90% of schools to keep their school premises free of dengue breeding sites through inspections conducted every Friday for 30 minutes.

Appropriate messages were disseminated through the channel mix of administrative mobilization/public relations/advocacy; community mobilization; advertising; personal selling and interpersonal communication; and point-of-service promotion. The M&E plan included monitoring during the planning and preparatory phase and during the implementation phase as well as pre- and post-intervention surveys. Evaluation of the COMBI plan was carried out in 2009 through key informant interviews (with supervisors of the implementers of the COMBI plan), focus group discussions (with the target audience), entomological surveys, and by testing the consistency of the messages. However, certain constraints such as lack of commitment, and paucity of human resources and funds, however, needed resolution for sustaining COMBI activities.

12. The Primary Health Care Approach to Dengue Prevention and Control

12.1 Principle of primary health care

Primary health care, or PHC, is a broad and comprehensive concept, and is defined as *"…essential health care based on practical, scientifically sound and socially acceptable methods and technology made universally accessible to individuals and families in the community through their full participation and at a cost that the community and country can afford to maintain at every stage of their development in the spirit of self-reliance and self-determination. It forms an integral part of both the country's health system, of which it is the central function and main focus, and of the overall social and economic development of the community.*[bi]

PHC, thus, is a multidisciplinary approach that encompasses a continuum of quality and comprehensive care – health promotion, disease prevention, treatment, and rehabilitation – by addressing a range of social, cultural, economic and environmental factors that cause ill health as well as those that sustain and maintain health. It is the first level of contact of individuals and the family and community with the national health system through a referral system, bringing health care as close as possible to where people live and work, and constitutes the first element of a continuing health-care process in a cost-effective and equitable[bj] manner.[185] It is applied as a public health tool that requires and promotes maximum community and individual self-reliance, self-determination and participation in the planning, organizing, operation and control of primary health care, making fullest use of local, national and other available resources.[bk] It also serves as the foundation of health systems strengthening.

PHC and Health For All (HFA) are part of the Alma-Ata (now called Almaty) Declaration of 1978[bl] that marked the commitment of Member States of the United Nations towards achieving a more equitable health status across the world, particularly in developing countries. More than three decades after the Declaration, there is growing realization that the concepts and approaches of PHC continue to remain valid. A Regional Conference on Revitalizing Primary Health Care was recently organized by the World Health Organization's South-East Asia Region in Jakarta, Indonesia, in 2008.[bm]

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bi Declaration of Alma-Ata. International Conference on Primary Health Care, Alma-Ata, (then) USSR, 6–12 September 1978. *(http://www.who.int/NPH/docs/declaration_almaata.pdf)*

bj WHO's definition of "equity in health" encompasses two different aspects: 1) Equity in health (health status) means *attainment by all citizens* of the highest possible level of physical, psychological and social well-being; and 2) Equity in health care means that health care is provided in response to the legitimate expectations of the people; health services are received according to need regardless of the prevailing social attributes, and payment for health services is made according to the *ability to pay*. (WHO SEARO. Equity in access to public health. Report and documentation of the Technical Discussions held in conjunction with the 37th Meeting of the CCPDM. New Delhi, 31 August 2000. New Delhi, WHO, 2000 (Document No. SEA-HSD-240).

bk Declaration of Alma-Ata. International Conference on Primary Health Care, Alma-Ata, (then) USSR, 6–12 September 1978 *(http://www.who.int/NPH/docs/declaration_almaata.pdf)*.

bl A result of a joint WHO-UNICEF International Conference on Primary Health Care held at Alma-Ata (now called Almaty), 6–12 September 1978.

bm WHO. *World Health Report 2008. Primary health care: Now more than ever. Geneva,* WHO, 2008. *http://www.who.int/whr/2008/*

The Millennium Development Goals that were adopted by UN Member States in 2000[bn] provided continuity to the values of social justice and fairness articulated at Alma-Ata in 1978 and further affirmed the central and pivotal position of health on the development agenda as a key driver of social and economic productivity and a route to poverty alleviation. One can consider the health-related MDGs as the principal mission or primary objectives of HFA till the target year of 2015. They also simultaneously serve as proxy indicators for HFA.

12.2 Primary health care and dengue prevention and control

The ultimate goal of controlling any epidemic disease including dengue is to prevent its transmission and contain the spread of the disease as soon as possible. The success of the efforts for prevention and control of dengue relies on the effectiveness of the initiatives to control the breeding sites of the vector by improving public and household environmental sanitation and water supply, and through sustained modification of human behaviour.[186]

This requires the entire gamut of public health activities, namely, health promotion, which is the process of enabling people across all socioeconomic groups to increase control over, and to improve, their health;[187] and disease prevention and treatment with appropriate technology along with rehabilitation. However, efforts to prevent and control dengue in the past have been constrained due to inadequate community participation[144] as well as lack of the necessary degree of intersectoral cooperation and service coverage, which are the core elements of PHC.

It has time and again been underscored that the PHC approach if applied effectively contributes to the achievement of desired health goals and objectives, especially when the success of a disease control programme relies heavily on community participation and intersectoral cooperation with non-health sectors in the prevention of disease, including vector control, and the treatment of the sick. PHC is, therefore, indubitably the right tool to ensure the effectiveness of strategies and related actions.

To secure and sustain community participation and intersectoral cooperation, the following activities should be carried out:

Community participation

Community participation involves "…active voluntary engagement of individuals and groups to change problematic conditions and influence policies and programmes that affect the quality of their lives or the lives of others".[188,bo] Community participation can lead to initiatives on the part of the community and allow members to assume "ownership" of the development process.[189]

Regarding DF/DHF control, community participation is extremely important as can be gauged from the fact that even those households which do follow the recommended actions for prevention may still harbour *Ae. aegypti* or other mosquitoes in their homesteads and, worse still, may suffer dengue infections if their neighbours do not participate in controlling domestic breeding sites. Members of such households may also get infected outside their homes or at their place of work or study. Therefore, the issue regarding vector control is not about whether source reduction is effective but whether and how community participation can be a part of that source reduction effort.[173,190]

whr08_en.pdf

bn United Nations General Assembly. Resolution 55.2. United Nations Millennium Declaration. 2000. *http://www.un.org/millennium/declaration/ares552e.pdf*

bo Refer to Chapter 11 on IVM for definition and additional details on community participation.

In rural areas, frontline public health workers working in peripheral health units play a significant role, with technical and material support from district and provincial authorities, in securing the participation from the community in dengue control.

In urban areas community lifestyle is quite different. Together with primary health-care services offered through organizations responsible for urban health such as health centres and health units in municipalities, the basic principles of health promotion such as health-promoting schools, healthy communities and cities, and healthy workplaces should be applied.

This is because, unlike in rural areas, most urban people are engaged in the formal sector or institutions such as schools, factories, offices and workplaces, marketplaces and the like. Furthermore, many of them migrate from rural areas to work in cities and live in slums where the environment and sanitary conditions are often poor or decrepit. Vector proliferation in urban areas in particular is often associated with human activities that aggravate the rate of deterioration of environmental sanitation. A change in human behaviour and lifestyle is, therefore, a pressing and felt need.

This can be achieved if individuals, families and communities are made aware of the detrimental effect that careless and irresponsible behaviour has on their health and are then empowered with the necessary skills. Securing community participation in urban areas is important for the success of the programme and requires a similar, yet different, approach from that adopted for rural areas. Adopting a more structured approach at various levels from the policy to the individual would be more appropriate for urban areas.

Once initiated, community participation requires continuous government and organizational support, failing which it will not last long. The government's responsibility towards developing health-care services and facilities is, therefore, not diminished. Community participation needs both guidance and active interest from the government and can be sustained only through the constant motivation that is derived from the successes of their joint efforts and/or with support from relevant organizations and agencies. The political will of the government is of vital importance in this connection. It is extremely important that the government should adopt community participation as integral to the national policy for promoting health development.

Community organization and social mobilization

Despite constraints,[bp] organizing and mobilizing the community and other community-level stakeholders is a critical element in an effective and sustainable dengue control programme. This entails several tasks:

- **Raising community awareness:**[bq] Use different communication channels and an appropriate media-mix such as local radio, community theatres, posters, leaflets, group sessions/civic forums, etc. to inform the community about the morbidity and mortality due to dengue in a particular area and elsewhere and the related economic and opportunity losses incurred by both the family as well as the community/country. How the benefits of the programme can be dovetailed with the needs and expectations of the people must also be explained to the community.
- **Initiating community dialogue:** The key steps should include: recognizing the dengue prevention and control issue(s)/problem(s); initiating a discussion among community members; clarifying perceptions to reach a common understanding; expressing individual and shared needs; and sharing a vision for the future that includes an ideal picture of how the community wants to see itself in the context of the dengue problem.

bp For additional details, refer to Chapter 11.
bq For additional details, see section on 'Health Promotion and Prevention Activities' below.

- **Identifying and involving community health volunteers/workers:** Identify and select community health volunteers/workers who will be instrumental to the success of the programme, and who will in particular galvanize the community into action. They will serve as health educators, communicators, problem-detectors and problem-solvers, community organizers, and leaders for health to enhance individual and family self-care and responsibility as integral components of everyday life.[185] They will also serve as the link between the community and the health workers at the peripheral health units of the health-care delivery system.

  Dengue control should evolve as a natural component of the overall mixture of health services that a community chooses for itself. This should not involve the "adding on" of new tasks for the community health volunteers/workers, which leave them exhausted and fosters programme inefficiency. *The issue of overburdening the community health volunteers/workers will not arise if the community is truly involved in the planning of and taking responsibility for their own health and environment*.

- **Identifying key stakeholders for local planning and actions:** With community health volunteers/workers taking the lead, local leaders – both formal and informal – should take part in the planning process so that their knowledge of the local culture and their experiences in mobilizing community action can be used to their advantage. The planning exercise may begin by motivating key stakeholders such as local administrative authorities, community and opinion leaders (village elders, religious leaders, teachers, women's group leaders, youth groups and civic organizations, traditional healers, etc.) and forming a local group/committee for planning and action following needs assessment.

  Ensure real community representatives are identified as leaders since they will serve as good role models and as change agents for the community in dengue prevention and control. Dialogue with local leaders to galvanize them to participate in dengue control should be undertaken through personal contact, group discussions and use of audiovisual materials. Interaction should generate mutual understanding, trust and confidence, as well as enthusiasm and motivation. The interaction should not be a one-time affair and should continue to achieve sustainability.

  The local committees should describe the importance of the uptake of interventions/services offered to the community and assist in building their capacity to identify their problems. The seriousness of the identified problems should be explained and that should include site/field visits for exposure. A sense of ownership among the local committees should be promoted and local resources mobilized as much as possible. Efforts should be made to grant recognition to the successes and best practices of local stakeholder committees by designating them as "model committees".

- **Empowering stakeholders by building capacity:** To facilitate the contribution of stakeholders to the programme, they should be empowered to possess necessary knowledge and skills, at least in the following:
  - Simple methods of planning and evaluation of dengue control, namely survey of larvae and different methods of larvicides, COMBI.[br]
  - With regard to leadership, many communities leave leadership in vector control entirely to professionals. This does not mean that the community lacks leadership from within itself. In fact, for primary health care to succeed, the existing and potential leadership pool must be enhanced. Local leadership may emerge from many sources, such as traditional healers and birth attendants, elders and religious leaders as well as from serving officials of the local community. Leadership development requires that the

br For additional details refer to Chapter 12.

health professional indentify and collaborate with local leaders. The community health worker is an important link in this process. Community-level management systems for acquiring, monitoring and distributing vector control supplies and equipment, appropriate action as well as timely case detection and proper treatment-seeking can grow from the development of local primary health-care leadership.

Baseline data collection

An assessment of current status tells the community where they stand in relation to the problem today.

Simple tools should be developed by the members of the planning committee with the help of health workers and supported by technical experts to collect baseline data on the nature and extent of vector problems, breeding sites, location of human habitats, disease outbreaks, the number of dengue cases which turned severe and complicated within a certain period, and sociobehavioural data related to disease transmission, treatment-seeking, etc. Both quantitative and qualitative assessments are necessary to get a comprehensive picture. Analysis of such data should be simplified to suit the group. Discussions on the results of the survey should be held among members.

Programme planning

Baseline data should be used in planning dengue control programme activities. The key strategies are:

- Set feasible objectives: These must be specific, measurable, achievable, realistic and time-bound, and should create a high level of individual/community motivation that is required for taking appropriate action to resolve problem(s).
- Determine appropriate strategies and tools including those for community education and mobilization, making use of stakeholder knowledge and experiences about the social, cultural and behavioural aspects of the community.
- Develop an implementation plan with clearly defined actions.
- Design a basic monitoring, evaluation and surveillance system.
- Establish indicators to measure progress and outputs vis-à-vis the objectives.
- Identify resource needs (materials, financial, equipment, supplies, expertise, etc.) and indicate those that can be procured locally as against those that have to be procured externally.
- Clarify roles and responsibilities of stakeholders including local committee members.
- Seek collaborative support and involvement from relevant agencies and voluntary organizations at the district and community levels.

For planning, it is critical to engage the community and stakeholders in various activities, as appropriate.

Implementation/community actions:

A specific workplan/timetable for each activity should be discussed among the community or stakeholders to achieve consensus, understand timelines and to determine who does what, when and how and with what kind of support from local health personnel. The more the community participates in such discussions and views the proposed actions as their own the more likely are they to take tangible and successful action. Any programme directed towards the community will not work without the essential elements of community awareness and community involvement at its planning and implementation stage.[191,192]

Achieving a consensus on action can at times lead to conflict between interest groups or reveal a degree of lack of commitment on the part of some groups. The leadership needs to explore options and evaluate them from the standpoint of conflict and its resolution.

The plan should cover the whole range of activities from health promotion and disease prevention – which include changing health behaviours and ensuring household and surrounding environmental sanitation – to monitoring the outbreak of disease, referring patients to the nearest primary care unit, and M&E of the programme using simple indicators such as household index, container index, number of cases, etc. Activities should be tailored to fit the community lifestyle and the prevailing social, cultural and economic conditions.

A key element that community actions need to keep in mind is the involvement of individuals who are the most vulnerable or most disadvantaged in the community. Not everyone will experience the problem(s) with the same degree of severity. For example, economically affluent families with means of personal protection and adequate access to quality heath care may not have to cope with health problems regularly and, therefore, perceive such problems to be individual issues. If any conflict arises, the leaders are to resolve it first before progressing with the problem. To resolve any conflict, more clarification may be needed or new leaders/stakeholders may have to get involved so that the majority can convince a reluctant minority to go along with them.

(a) Promotion and prevention activities:

From a health promotion perspective, gaining the trust of the entire community is often difficult, and without trust it is hard to convince people to adopt healthier lifestyles.[193] The desired changes in a community as well as in the supportive structures necessary for community-based health promotion are often slow. There are a number of changes that are frequently resisted and these are:[194]

- changes that are not clearly understood;
- changes that the community or their representatives have no part in bringing about;
- changes that threaten vested interests and security;
- changes advocated by those whom the community do not like or trust; and,
- changes that do not fit into the cultural values of the community.

Community capacity should be developed and fostered with different components of the community working together as well as through capacity-building and the involvement of health promotion workers as mentioned above.

Health education and empowerment:[bs]

Health education should raise awareness about the magnitude, severity, transmission and control of the disease, and initiate/sustain appropriate behavioural change[bt] at both the community and individual levels. The behaviour change needed for vector control – which often involves changing old and familiar habits or methods with regard to water storage, solid waste disposal (junk, etc.), proper personal protection measures and action to be taken when having fever – should be aimed at. The broad categories of factors that may influence individual and community health behaviours must be taken into account when planning for health education activities. These include knowledge, beliefs, values, attitudes, skills, finance, materials and time, and the influence of family members, friends, co-workers, opinion leaders as well as the health workers themselves.

bs For details, refer to chapter on communication on behavioural impact.
bt For details, refer to chapter on communication on behavioural impact.

Health education should use locale- and context-specific communication channels (such as mass media including local radio stations, cable TV networks, newspapers; community outreach programmes such as community/group sessions by community health volunteers/workers, theatre/folk media, public announcements; interpersonal communication; and posters, leaflets, activity booklets with guides, etc.) in a synergistic manner.

Different methods of education and skill development such as group discussions, slide presentations, demonstrations, role play, role models, participatory learning and problem solving should be used to address factors influencing individual and community health behaviours. In other words, an understanding of the local sociocultural and economic characteristics, together with consultation with stakeholders should make it possible to select suitable methods for health education.

In addition to improving knowledge and awareness, the necessary skills in dengue prevention and control – such as elimination of breeding sites, methods of larvicide use, and actions to be taken during fever – should be inculcated among the target groups. At the community level, the task to increase people's awareness and develop necessary skills for the desired environmental and sanitation changes can be effectively shifted to the women's groups, self-help groups, NGOs including faith-based organizations, formal and informal community leaders, community health volunteers, school students/teachers, and the like. Targeting children and their families to eliminate vector breeding at home and at school together with the rest of the community should be emphasized.

Health education can be implemented in a campaign mode and/or as part of a routine programme. The campaigns/routine programmes could be implemented in an integrated manner with other necessary community development programmes, especially those with health implications. The activities should be intensified before and during the period of dengue transmission while continuing on a regular basis to reinforce message dissemination for sustaining appropriate actions. This is quite a challenging endeavour.

Campaigns: Organize "clean-up" campaigns two or more times a year to control the larval habitats of the vectors in public and private areas of the community. One such campaign should be timed prior to the transmission season. These could be coincided with significant national or community events such as the observance of the "National Day", 'Earth Day', other religious days and so on. These campaigns should be supported by appropriate communication activities for the dissemination of messages designed to change individual behaviour or promote collective action.

Integrated programmes: Community programmes for dengue prevention and control could be integrated with other priorities of community development. Where municipal services related to refuse collection, waste water disposal, provision of potable water, etc. are either lacking or inadequate, the community and partners could be mobilized to improve such services. At the same time larval habitats of vectors can be reduced, thereby contributing to the overall effort.

Some key factors for the success of such programmes include the use of the "Champion", who is considered to be the "catalyst" or "change agent" or "key influencer". Community involvement in planning and implementation with the support of health personnel and related sectors, extensive publicity via various communication channels and follow-up evaluations are also of crucial importance. Children should be encouraged to participate from the planning stage till the end. Participation by municipal authorities in cities and appropriate local bodies in rural areas should be promoted. Novel incentives and reward schemes for those who participate in community programmes for dengue control should be designed to recognise their services and motivate them into continual engagement.

(b) Surveillance (vector and disease) and treatment

About once a week trained community health volunteers/workers and/or community leaders and/or schoolchildren and teachers should visit households, schools, etc. in their respective catchment areas to check mosquito breeding sites and apply control interventions as locally appropriate. Other preventive behaviours such as using bednets or screens on doors and windows and mosquito repellants, and adoption of suitable water-storage and household and environmental sanitation measures should also be discussed with the householders.

During the period of dengue transmission, the community health volunteers/workers and/or community leaders should visit households to make sure that any fever case, particularly children or at-risk, are properly taken care of and referred on time to the primary health care centre or other referral health facilities for proper treatment. Communication and transportation for referring patients must be ensured. Positive cases must immediately be reported to the agency concerned and action taken to control the disease.

(c) Containment of disease

In an outbreak of dengue, health staff at the peripheral health unit together with community health volunteers will be notified to join the Surveillance and Rapid Response Team as members to carry out disease investigation and control measures. Health education must also be imparted along with case investigation and insecticide spraying.

(d) Monitoring and evaluation

People are willing to continue their activities if they see the results of their efforts. Therefore, evaluation of the prevention and control programme is an important element in making the programme sustainable. A monitoring system should be designed to collect and analyse necessary data (entomological and epidemiological) as well as review ongoing programme activities through supportive supervision. Feasible indicators should be set to measure progress in outputs and outcomes. Participation by the community in monitoring and evaluation should be ensured. The results are also to be shared with the community.

In urban areas, efforts should be made to set up a databank with all the information obtained from surveys and the studies carried out in areas that either have foci of infestation or are capable of generating them. The databank should also contain information on the underlying causes of such foci, vector density per residential unit, block or hectare, seasonal fluctuations and oscillations, and the relationship between indicators and the incidence of diseases associated with or transmitted or borne by such vectors.

(e) Social support and social network

In order to make the programme sustainable, social support from community health volunteers/workers should be provided to the community on a regular basis. Social networks should be encouraged about joint activities to both sustain and expand the dengue control programme.

Intersectoral collaboration

The dengue control programme cannot be successfully implemented or accomplished by the health sector alone. Contributions from other sectors (non-health departments of the governments such as education, public works, information and mass media, environment, urban and rural development and the like, and nongovernment organizations, the private sector, and local self-government institutions such as the municipalities) are also required to participate and/or contribute to make the programme effective and sustainable.

Intersectoral collaboration is another key element of primary health care in addition to community participation. Hence, any programme should ensure that the health sector interacts with sectors involved with national development or that impact the health and well-being of the people, in both urban and rural areas. The Ministry of Health must have a focal point responsible for coordinating and convincing other related sectors to take health aspects into consideration during their policy formulation. Intersectoral task forces or committees that meet periodically for strategic planning, implementation and oversight should be formed as well. High-level intersectoral meetings that are held at least once a year are useful in establishing the principle of sustainable intersectoral cooperation.

Intersectoral collaboration is and should be an important feature of vector control programmes.[bu] It is well known that the activities of other sectors and the community contribute to the breeding and spread of vectors and that is why such collaboration can help limit and control vectors in both rural and urban areas. Improved intersectoral collaboration requires that vector control be better integrated in the developmental plans of other sectors, or in other words, incorporated into healthy public policy. *[Healthy public policy aims at creating a supportive environment to enable people to lead healthy lives. In the pursuit of healthy public policy, government sectors concerned with trade, agriculture, education, industry, and communications, etc. need to take into account health as an essential factor when formulating policy. These sectors should be accountable for the health consequences of their policy decisions: Second International Conference on Health Promotion, Adelaide, South Australia, 5-9 April 1988]*. Health development must not compete with the social and economic goals associated with rural, industrial and urban development; it must evolve as an essential requirement on its own.

One starting point for intersectoral collaboration is the exchange of information between sectors to determine priorities. Since vector propagation is linked with planned activities such as road-building, the opening up of new land for agriculture and urban development and the like, it is possible to evolve an information system that graphically depicts and forecasts important developments.

Vector control in urban areas should also include urban planning. The planning of urban settlements and planned urbanization can help enhance the quality of life on the whole as well as the health and general well-being of urban populations and that of migrants to the cities. Planning should be undertaken by a multidisciplinary group that can provide the necessary guidance as well as establish guidelines for consistent and adequate policy decisions.

Three distinct situations associated with vector proliferation need to be considered in the planning process: (i) the construction of a new city; (ii) the expansion of a neighbourhood or an existing part of a city; and (iii) the growth of small pockets in different parts of the city. It is easier to plan for a completely new city and it is moderately difficult to forecast the needs of a new neighbourhood or sector of a city, but it is extremely difficult to foresee what preventive or coercive measures will be needed for small areas. The multidisciplinary group in charge of urban planning or of studies to serve as the input for urban planning activities must include physicians, public health personnel, vector control specialists, sanitary engineers and architects specialized in urban planning.

The ministries of health and urban development as well as the municipalities should organize regular meetings with architects, builders' sssociations and institutions such as RWAs (residents' welfare associations); and enact and implement building by-laws/act, civic by-laws for preventing mosquito breeding conditions. Public health engineers must be involved to design mosquito-proof water-coolers, lids for water tanks and such utilities as well as initiate technology exchanges for effective and wide implementation. Health impact assessment of all development projects must also be undertaken by the authorities concerned.[bv]

bu Also refer to Chapter 10.
bv For additional detals refer to Chapter 10.

In community settings in urban and rural areas, the organizations responsible for providing health-care services – such as the ministry of health or the municipality – must ensure that quality primary health-care services are accessible and available to the community and effective referral systems from the community to the health-care unit are in place. The ministry responsible for public works and their municipal counterparts in urban areas and the ministry of rural development and allied entities, including nongovernmental organizations, in rural areas should be involved in preparing appropriate development programmes that preclude mosquito breeding. They can contribute to source reduction by providing a safe and dependable water supply, adequate sanitation and effective solid waste management. 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 run-off control for new housing developments, or forbid open surface wells.

In communities, health personnel should carry out a survey and map out the area to familiarize themselves with it and identify key stakeholders and **NGOs** working in the community there and secure their cooperation for the dengue control programme. NGOs can play an important role in promoting community organization and participation and implementing environmental management for dengue control. This will most often involve health education, breeding source reduction and housing sanitation improvement.

Community NGOs may even be informal neighbourhood groups or formal private voluntary organizations, service clubs such as Rotary or women's clubs, churches or other religious groups, or environmental and social action groups. If needed, they should be trained by staff of the Ministry of Health in breeding source reduction methods, recognizing signs and symptoms of dengue fever, undertaking appropriate action thereof, and other related issues. They can help in mobilizing and working with the community to collect discarded containers, clean drains and culverts, fill depressions, remove abandoned cars and roadside junk, and distribute sand or cement to fill tree holes. They may also play a key role in the formulating recycling activities and removing discarded containers from yards and streets. Such activities must be coordinated with the environmental sanitation services.

In schools, a health education component targeted at schoolchildren should be developed and appropriate health messages devised and communicated. It must be kept in mind that the school is an excellent medium to reach out to the main target groups, children and families (*Box 28*).

Health education models can be jointly developed, tested, implemented and evaluated for various age groups by the Ministry of Education and Ministry of Health. Such cooperation between the two ministries will facilitate health personnel to work with schools in dengue control through the principles of primary health care and health promotion in schools. Several activities should be encouraged, such as monthly cleanliness drives in different neighbourhoods supported by give-away BCC materials (leaflets, hand outs, etc.), and projects, debates and competitions.

The ministry of education should consider the inclusion of topics and practical work related to dengue prevention and control in the curriculum and the printing of appropriate messages in textbooks, as appropriate. To make the programme sustainable, teachers must be equipped with the necessary knowledge and skills in dengue control through training and by working closely with health personnel so that they will be able to independently continue the programme in the future.

The concept of volunteers and peer support can be applied with schoolchildren to encourage them to actively participate in the programme. These young volunteers should be provided with leadership and dengue control training so that they can be efficient as change agents for others in their schools and communities. As part of leadership training and enhancement of self-efficacy, these children should be involved in planning, implementing and evaluating the programme.

At the workplace/factory/industry, health personnel of the area should work with the management/unions of organizations to put dengue control through the concept of healthy workplace. Raising the knowledge and awareness levels about the importance of dengue control could be done through the "Champions" who are easily recognized by the community and command respect for their capacity to inform, convince, reinforce and advocate on the basis of evidence. However, convincing the management is the most challenging task because the programme may eat into the working hours of employees and improvement of waste management and sanitation can cost both time and money. Hence, government policies, laws and regulations concerning environmental sanitation and sanitizing workplaces and industries will be needed.

Once agreed by the management of the workplace, primary health care and healthy workplace can be effectively applied. In a large organization, there is at least one occupational health personnel who is responsible for the health and safety of employees. Government health personnel should work closely with the workplace authority, occupational health personnel, and leaders of employees in matters of planning, implementing and evaluating dengue control programmes. For sustainability of the programme, these stakeholders should be empowered with the necessary knowledge and skills, including leadership skills, to enable them to completely take over the programme in the future while retaining technical support from government health personnel.

Examples of successful community participation and intersectoral involvement —the core elements of PHC approach for dengue control — are illustrated below (*Box 40*).

Box 40: Dengue control through community/intersectoral involvement in Thailand, Malaysia and Cuba

In **Thailand**,[183] PHC was initiated in 1980 and currently there are has 900 000 village health volunteers (VHVs) with one VHV for every 10 households. The VHV is selected by community and health staff and trained for two weeks. After that self-learning with the help of books and other media is encouraged. The key roles and responsibilities of VHVs for dengue control include: IEC by means of interpersonal communication, village-level broadcasts, etc. supported by larval surveys and subsequent control with temephos, "cleaning day" campaigns, as well as dengue fever control by advising patients to take essential drugs and refer to hospitals if there is no improvement. Warning the community about disease outbreaks as informed and screening case(s) in respective catchment areas; coordinating with school or housewives' groups to take care of children; producing herb-based repellents (for example, citronella); and conducting monthly meetings with health staff to exchange information on situations and new IEC materials are other responsibilities.

According recognition to VHVs to sustain their commitment is a critical aspect of the programme. In Thailand, health volunteers are identified in the workplace, schools, and other places. The local administrative organizations that have the financial resources and regulations to support dengue control encourage VHV activities. The Bangkok Municipal Administration (BMA) has also taken a lead role to control dengue in the national capital. Generating public awareness, keeping the environment clean and eliminating breeding places as well as space-spraying in outbreak situations are the major responsibilities.

In **Malaysia**[178] (Johore State), a campaign motivated householders to seek prompt diagnosis for any fever, destroy any larval breeding site found around their premises, and organize voluntary teams to inspect and control larval breeding sites in public spaces such as community halls, parks and vacant lots. Dengue volunteer inspection teams (DeVIT) were formed in 48 localities with 615 volunteers. During the three-month campaign, DeVIT teams proferred advice to 100 956 people, distributed 101 534 handouts, and inspected 1440 vacant lots.

The campaign resulted in a dramatic drop in the occurrence of dengue in the district; three months after the campaign tracking surveys revealed that 70% householders were still inspecting their household premises regularly. Today, 95% of DeVIT volunteers continue with their work. The government of the state of Johore has decreed that the campaign be implemented throughout the state. The experience showed that a group of committed and dedicated people can plan and execute a project; and that communities and households will readily get involved if the behavioural targets set are reasonable and achievable. However, sustaining the interest of the volunteers is fundamental.

In **Cuba**[195]achieving sustainability is one of the major challenges currently in disease control programmes. In 2001–2002, a community-based dengue control intervention was developed in three health zones of Santiago de Cuba. New structures (heterogeneous community working groups and provincial/municipal coordination groups inserted in the vertical programme) were formed, and constituted a key element to achieve social mobilization. In three control zones, routine programme activities were intensified. Sustainability of the intervention strategy over a period of two years following the withdrawal of external support was evaluated.

The interventions – evaluated through larval indices and behavioural change indicators – were found to have been maintained during the two years of follow-up. In the intervention area, 87.5% of the water-storage containers remained well covered in 2004 and 90.5% of the families continued to use a larvicide correctly as against 21.5% and 63.5% respectively in the control area. The house indices declined from 0.35% in 2002 to 0.17% in 2004 in the intervention area, while in the control area they increased from 0.52% to 2.25%.

Institutionalization of the intervention was reaching a saturation point by the end of the study. Key elements of the intervention had lost their separate identity and become part of the control programme's regular activities. The host organization adapted its structures and procedures accordingly. Continuous capacity-building in the community led to participatory planning, implementation and evaluation of the *Aedes* control activities. It was concluded that in contrast with intensified routine control activities a community-based intervention approach promises to be sustainable.

Strengthening of health-care services

Medical and public health services provided by the government (the health sector) and the private sector should be assessed and strengthened since improved community participation and intersectoral collaboration expect robust supply-side systems.

13. Case Investigation, Emergency Preparedness and Outbreak Response

13.1 Background and rationale

Dengue outbreaks evolve quickly, requiring emergency actions to immediately control infected mosquitoes in order to interrupt or reduce transmission and reduce or eliminate the breeding sites of the vector mosquito, *Ae. aegypti*. In order to meet such emergencies, it is essential that persons at all levels, including individuals, the family, the community and the government, contribute to preventing the spread of the epidemic.

Two major components of the response to a dengue outbreak are:

(1) Emergency vector control to curtail transmission of the dengue virus as rapidly as possible.

(2) Early diagnosis and appropriate clinical case management of dengue to minimize the number of dengue-associated deaths.

These two components should be implemented concurrently. The response will also differ depending on the endemicity in countries.

For endemic countries, the overall aim is to reduce the risk of dengue outbreaks and strengthen control measures for any future outbreak in order to minimize the clinical, social and economic impact of the disease.

Receptive countries (i.e. dengue vectors present without circulating virus), should focus on strategies for risk reduction. These should include rapid investigation of sporadic cases (clinically suspected or laboratory confirmed) to determine whether they are imported or locally-acquired, monitoring of vectors and their abundance (particularly in regions with recorded or suspected cases), social mobilization, and environmental management efforts. Once a locally acquired case is confirmed, the response may be escalated to epidemic response to prevent further spread and/or ensure interruption of transmission.

13.2 Steps for case investigation and outbreak response

The following are the essential steps for case investigation and response:

Step One: Designation of an investigation team (see Annex 11)

Prior to conducting an outbreak investigation, it is important that a multidisciplinary team including epidemiologists, entomologists, microbiologists and social scientists, is designated. The team should take up the following tasks:

- Technical: This involves the process of planning for laboratory materials, specimen collection, and storage and transportation techniques. A sample case investigation form may be prepared.
- Logistics: Administrative procedures including travel plans and other arrangements should be worked out. Investigators should establish and build partnerships whenever possible. The team should plan for further necessary steps to deal with media and other communities in the locality.
- Coordination: Before starting the investigation all team members should agree on the plan and their roles stipulated and responsibilities.

Step Two: Verification of the outbreak

The investigation team should visit the area as early as possible to collect information on cases, their clinical signs/symptoms, history of exposures and other relevant epidemiological/entomological and laboratory information (where possible) to substantiate the outbreak.

Step Three: Case definitions and additional case-finding

Case definition as mentioned in *Box 8* should be applied to all suspect cases to decide how they should be classified. Efforts should be made to find additional cases from health institutions and community-based investigation and to determine whether clustering exists.

Step Four: Standard case investigation and methods of control

Standard investigation includes completion of standard investigation forms *(Annex 12)* and analysis of dengue laboratory reports.

- Facility-based (hospital/medical institution/clinics, etc.) investigation:[bw]
  - Contact the medical provider who diagnosed or ordered the testing of the case and obtain the following information. This includes copies of hospital/clinic records, etc.

    Note: If the physician submitted samples to any appropriate laboratory facility, the case investigation form may already be completed or started. Try to obtain a copy.
  - Identify if the patient was ill with symptoms of dengue fever.
    - Refer to *Box 8*.
    - Record onset date of first symptom.
  - Examine the laboratory testing that was done; if not yet reported.
    - Record date of serum specimen(s) and/or tissue (specify) collection.
    - Record or obtain copies of serology results and virus isolation and PCR tests, if done.
  - Collect demographic data and contact information of case [full name, date of birth, country, sex, race/ethnicity, home address, occupation and work address, relevant phone number(s)].
  - Record hospitalization details: location, admission and discharge dates.
  - Record outcomes: recovery or date of death; any mental status changes.

bw Adapted from: *Dengue Fever, Dengue Haemorrhagic Fever, Dengue Shock Syndrome Investigation Guidelines. Version 01/ 2010. Kansas, USA.*

- Community-based investigation:[bx]
  - Interview the case or proxy to determine source and risk factors; focus on incubation period of two weeks prior to illness onset.
  - Travel history:[by]
    - Travel outside town/city: list the places visited and dates.
    - Travel outside country: list country, date of departure and return (to the country of origin).
    - Any exposure to mosquitoes (include dates and places).
    - Collect information from case for the **contact investigation** (see below).
  - Investigate epidemiology links among cases (clusters, household, co-workers, etc.)
- Contact investigation:[bz]
  - Contacts are those who have exposure. Exposure is defined as:
    - travel to a dengue endemic country or presence at a location with ongoing outbreak within previous two weeks of dengue-like illness; or
    - association in time and place with a confirmed or probable dengue case.
  - Identify other individuals who may have had contact with the source in the two weeks prior to the case becoming ill to find unreported or undiagnosed cases.
  - If travel by the case occurred as part of a commercial travel group, investigate travel companions.
- Isolation, work and day care restrictions:
  - Follow blood and body fluid precautions as prescribed by physician.
  - Prevent access of mosquitoes to the case until fever subsides through the use of screened sickrooms, spraying with insecticides, and bednets.
- Contact management:
  - Educate all contacts on the symptoms of dengue fever.
  - Investigate symptomatic contacts with dengue-like illness as suspect cases, collect acute and convalescent specimens and coordinate testing at the appropriate laboratory facility.
  - Symptomatic contacts should be instructed to rest, drink plenty of fluids, and consult a physician. If they feel worse (example, develop vomiting and severe abdominal pain) 24 hours after the fever declines, they should immediately seek medical evaluation with their physician or hospital/clinic.

Step Five: Laboratory and environmental information

Laboratory confirmation is essential for establishing the aetiology of the disease causing the outbreak.[ca]

bx Adapted from: *Dengue Fever, Dengue Haemorrhagic Fever, Dengue Shock Syndrome Investigation Guidelines. Version 01/2010. Kansas, USA.*

by Travel to an active dengue fever area is a **crucial** element.

bz Adapted from: Heymann, D. L. (Ed.): Control of Communicable Diseases Manual. 18th edition. 2004. American Public Health Association. Washington DC, USA.

ca It is important to have an idea about what specimens will be collected, stored and shipped to the appropriate laboratory. Refer to Chapter 5.

It is not necessary to confirm the diagnosis of all cases detected during an outbreak. It is sufficient to confirm diagnosis in a sample of cases at the beginning, the interim period and the resolution of the outbreak. Containment measures should not be delayed by lack of laboratory diagnosis.

Ae. aegypti is the primary vector, which is a container habitat species and well entrenched in urban areas. Entomological indices of container index (CI), house or premise index (HI) and Breateau Index (BI) should be determined for the affected areas. Similarly, types of containers, both indoors and outdoors, should be mapped for control of vector breeding.

Step Six: Communication with authorities concerned and recommendation of control measures

Findings should be communicated to appropriate decision-makers and control measures recommended. The following action is to be carried out by local health authorities.

- An Emergency Action Committee (EAC) (see Annex 11) may be constituted to coordinate activities aimed at emergency vector control measures and management of serious cases. The committee may comprise administrators, epidemiologists, entomologists, clinicians and laboratory specialists, social scientists, school health officers, health educators and representatives of other related sectors including civil society. The functions of the EAC will be to:
  - take all administrative actions and coordinate activities aimed at the management of serious cases in all medical care centres and undertake emergency vector control measures;
  - draw urgent plans of action and resource mobilization in respect of medicines, intravenous fluids, blood products, insecticides, equipment and vehicles;
  - form a rapid action team comprising epidemiologists, entomologists and laboratory specialists to undertake urgent epidemiological investigations and provide on-the-spot technical guidance required and logistic support;
  - liaise with inter-sectoral committees to mobilize resources from non-health sectors, namely Urban Development, Ministry of Education, Ministry of Information, Legal Department, Water Supply Department, Waste Disposal Department and share and disseminate information for the elimination of the breeding potential of *Ae. aegypti*; and
  - interact with the media and NGOs for health education and community participation.

Step Nine: Implementation of control measures

Control measures should be initiated as soon as the outbreak is verified even before an epidemiological investigation is started or completed. They usually direct against one or more segments in the chain of transmission (agent, source, mode of transmission, portal of entry or host) that are susceptible to intervention.

For control of epidemics, vector control is considered to be one of the important strategies to interrupt or reduce transmission. Adult mosquitoes can be controlled by the use of chemical insecticides. It should be emphasized, however, that rapid and effective source reduction for elimination of breeding sites of vector mosquitoes will achieve the same results. Moreover, larval control is more economical and provides sustainable control by eliminating the source of newly-emergent adult mosquitoes. Chemical space sprays are not effective in most of the conditions and it is rare that an epidemic will be controlled by using these methods. Because of their visibility, however,

people think that the government is active in disease control when space sprays are carried out. This often creates a false sense of security and prevents/slows down community as well as individual efforts for vector control. Hence, communities need to be engaged appropriately. Indoor space spray with pyrethrum 2% extract (0.2% ready to spray solution with kerosene oil) is applied where the case(s) is/are detected and in surrounding houses.

Public education must continue to reinforce how important it is for people to seek medical attention if they have dengue symptoms, reduce larval habitats and use options for personal protection.

During an epidemic the aim of risk communication, generally through the media, is to build public trust. It is done by announcing the epidemic early, communicating openly and honestly with the public (transparency), and particularly by providing accurate and specific information about what people can do to make themselves and their community safer.

This gives people a sense of control over their own health and safety, which in turn allows them to react to the risk with more reasoned responses.[35] In endemic countries, involving the media before the occurrence of the seasonal increase in dengue enhances the opportunity to increase public awareness about the disease and the personal and community actions that can be taken to mitigate the risk.

Step Ten: Follow-up of implementation of control measures

It is important to follow up and ensure consistency of implementation control measures and assess the effectiveness of control measures. An absence of new cases for at least two incubation periods of the disease under investigation could suggest that the outbreak is subsiding. The local health authorities in consultation with stakeholders can decide when to declare the outbreak to be over.

14. Monitoring and Evaluation of DF/D HF Prevention and Control Programmes

It is essential to monitor and evaluate the progress of DF/DHF prevention and control programmes. They enable the programme manager to assess the effectiveness of control initiatives and must be continuous operational processes.

The specific objectives of programme evaluation are to:

- measure overuse progress and specific programme achievements;
- detect and solve problems as they emerge;
- assess programme effectiveness and efficiency;
- guide the allocation of programme resources;
- collect information needed for revising policy and replanning interventions; and
- assess the sustainability of the programme.

14.1 Types of evaluation

There are two types of evaluation:

- Monitoring.
- Formal evaluation.

Monitoring

Monitoring or concurrent evaluation involves the continuous collection of information during programme implementation. It allows immediate assessment and identification of deficiencies that can be rectified without delaying the programme's progress. Monitoring provides the type of feedback that is important to programme managers. Most monitoring systems follow the quantum and timing of various programme elements such as activities undertaken, staff movements, service utilization, supplies and equipment, and budgeting.

Focus should also be given to the process of implementation of the dengue control strategy in time and space and the quality of implementation, seeking reasons for successes and failures. Monitoring should be undertaken by persons involved in the programme at various levels. This exercise by programme managers will give a better and deeper understanding of the programme's progress, strengths and weaknesses. The information collected should help programme managers strengthen the weaker links and optimize output.

Formal evaluation

In addition to regular monitoring, which is generally built-in, there is also a need for more formal evaluation at different intervals to obtain a precise picture of the progress of the programme. This type of evaluation is even more essential when the programme is failing to achieve its targets or goals or when it has become static. This type of special evaluation should be done systematically and should take into account all programme elements. The main idea of such a study is to determine whether the programme is moving on course towards its targets and goals, to identify new needs – particularly for increased inputs (e.g. – additional manpower, money, materials, IEC activities, capacity-building) and to identify operational research areas for maximum operationalization. Formal evaluation, therefore, should systematically assess the elements outlined below. However, the evaluation can cover one or more other processes depending on the objectives of the evaluation.

- Evaluation of need, i.e. evaluation of the relative need for the programme.
- Evaluation of plans and design, i.e. evaluation of the feasibility and adequacy of programme plans or proposals.
- Evaluation of implementation, i.e. evaluation of the conformity of the programme to its design. Does the programme provide the goods and services laid down in the plan in terms of both quality and quantity?
- Evaluation of outcomes, i.e. evaluation of the more immediate and direct effects of the programme on relevant knowledge, attitudes and behaviour. For training activities, for example, outcomes may relate to the achievement of learning objectives and changes in staff performance.
- Evaluation of impact, i.e. evaluation of the programme's direct and indirect effects on the health and socioeconomic status of individuals and the demography of the community.

14.2 Evaluation plans

An evaluation plan should have realistic and measurable targets. With this proviso, the development of an evaluation plan consists of the following steps:

- Clarification of the objectives of the evaluation: these must be agreed upon by all concerned.
- Identification of the resources available: there must be sufficient resources to collect the data on the scale envisaged and turn that into useful information.
- Selection of the type of evaluation: once the purpose of the evaluation is clear, it is necessary to decide the type of evaluation and the depth of information required.
- Selection of indicators: a good indicator is directly related to programme activities and anticipated outcomes. Therefore, indicators chosen should be limited in number, readily and uniformly interpretable, and operationally useful. For comparison purposes, use of standard indicators will introduce consistency into programme reviews and allow comparison over time and among countries. Although there are many ways of classifying indicators, one useful way is according to the programme structure outlined in *Box 41*. Thus, there can be input, process, outcome and impact indicators.
- Formulation of the detailed evaluation plan: the detailed plan should include the objectives, methods, sampling procedures, source of data and methods of data analysis to be used as well as budgeting and administrative arrangements. It should also give details of staff responsibilities for each activity, the reporting mechanism, and the strategies to ensure that results are used for programme replanning and implementation.

- Collection of data: the objective of this step is to ensure that procedures are followed in such a way that data are collected in a reliable and timely manner.
- Interpretation and analysis of data: the decisions about the main approaches to data analysis will have been made when the indicators are selected and the detailed plan formulated.
- Re-planning: at this step the results of the evaluation are fed back into the managerial process. Unfortunately, it is often this re-planning step that is done the least correctly.

Various aspects of programme that can be monitored and evaluated are presented in *Box 41*.

Box 41: Aspects of programme that can be evaluated

In *Box 42*, a scheme is suggested to identify expected results pertaining to any dengue prevention and control programme component (example, IVM[146]) and decide SMART[cb] indicators for monitoring and evaluation of targets, which in turn, will require the development or use of available methods/ tools.

Box 42: M&E framework

Expected results	Activity	Objectively verifiable indicators	Means of verification	Targets		Assump-tions/risks	Resources required
				Year 1	Year 2		
1.		1. Process indicators					
		2. Outcome indicators					
		3. Impact indicators					

14.3 Cost-effective evaluation

In most countries of the Region, it is difficult to estimate how much money dengue prevention and/ or control programmes use up annually. Often, dengue or *Aedes* control programmes function as branches of malaria control programmes 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 from 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, therefore, important that economic factors be considered during the reorganization or strengthening of dengue control programmes. Information of this nature is essential for: planning, evaluating cost-effectiveness of individual control measures, comparing

cb specific, measurable, achievable, relevant, time-bound.

different control measures, and evaluating new methods. Examples of types of cost estimates that should be obtained are described below.

(a) Vector control costs

Operational costs: It is not enough to merely estimate the quantities of insecticide required. Costing should begin with the size of the population to be protected, the number of premises or extent of the area to be treated, as well as the personnel requirements (at all levels) based on the frequency of application. Personnel costs include expenditure on training, safety equipment, and per diem or overtime where applicable.

Initial capital costs for equipment and on depreciation, and/or shared usage with other programmes must also be considered. Operational costs, especially for ULV space spraying, should include machinery and vehicle maintenance, regular 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 involves costs.

Environmental management: Source reduction programmes are often considered 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 of teachers, etc. may involve considerable costs. Some of these costs can be covered by other sectors such as education (municipal or private) and such collaboration should be encouraged.

Environmental management campaigns, especially clean-up campaigns, may fail due to lack of transport support and inadequate facilities for solid waste disposal. Communities, especially in cities, need either to invest in such equipment or make arrangements to rent or borrow them from other sources. As with chemical control, environmental management programmes must be evaluated and the vector and disease data organized and analysed. All of these activities involve costs.

(b) Laboratory surveillance

Most national laboratories that perform serology or virus isolation for other agents (measles, polio, etc.) can also include dengue. The cost of the dengue component must be adequately assessed based on an analysis of the number of samples processed, the cost of 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.

(c) Coordination with hospitals and medical supplies

In addition to coordination among its component parts, the programme requires coordination between curative and preventive services and these expenses should be recognized. An information exchange network is also required. In order to meet the potential for epidemic situations, hospital supplies and equipment must be readily available and be replaced and/or updated regularly. Each country should estimate the costs associated with individual case management. Through cooperation with and information from neighbouring countries and international organizations, countries must estimate its requirements on an annual or biennial basis.

(d) Surveillance

Guidelines for entomological and epidemiological surveillance methods are given in the chapter on surveillance. These can be used as a framework to estimate 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, includes expenditure for collecting and processing samples in the field.

(e) Community participation, health education and communication costs

In addition to the costs that have already been mentioned, liaison must be established with community groups. This is in order to provide technical assistance where required and to determine how the health authorities can assist these groups with their individual and collective efforts. Health education and communication activities will play a significant role in community participation efforts. Consequently, it is extremely important to estimate their cost. The calculation of the actual costs of health education, communication and community participation should also be made on an annual basis.

(f) Social and economic impact[cc]

The social and economic burden of DF/DHF is another element to be considered when determining the cost-effectiveness of DHF control. In a 1995 study carried out by the Faculty of Tropical Medicine of Mahidol University in Thailand,[196] in collaboration with the Faculty of Economics of Chulalongkorn University (Thailand), several parameters [treatment-seeking behaviour, direct impact, i.e. cost of the illness of patients (average 7.9 days) and time-cost spent by parents/caretakers (average 9.5 days), and indirect impact due to disruption of family life resulting in increased expenses] were identified. From the provider side, expenditures for the hospitalization of DHF patients included drug, laboratory and nursing costs and the cost of prevention and control. In a recent study in Thailand, weighted average of direct patient cost (including travel, food, lodging and opportunity) was estimated at US$ 61 per case excluding the cost of the government component of services in hospital.[197]

Another approach is to measure the disability-adjusted life years (DALYs) associated with dengue infection. A study in Puerto Rico showed a constant increase in the DALYs associated with dengue infection from 1984 to 1994.[198] Surprisingly, the DALYs associated with dengue infection in Puerto Rico were of the same order of magnitude as the DALYs relating to a number of other infectious diseases in Latin America, including malaria, tuberculosis, sexually transmitted diseases (excluding HIV/AIDS), hepatitis, the childhood cluster and the tropical cluster.

A more recent[199] study on the economic impact of DF/DHF at the family and population levels, accounting for the direct cost of hospitalization, indirect costs due to loss of productivity, and the average number of persons infected per family, observed a financial loss of approximately US$ 61 per family, which was more than the average monthly family income in Thailand at that time. The DALYs were calculated using select results from a family-level survey, and resulted in an estimated 427 DALYs/million population in 2001. This figure was of the same order of magnitude as that of impact of several diseases that were given priority in South-East Asia, such as malaria, meningitis, hepatitis and the tropical cluster (trypanosomiasis, Chagas disease, schistosomiasis, leishmaniasis, lymphatic filariasis and onchocerciasis).

cc For further reading: Finsterbusch, K. and Wicklin III, W.A.V. (1989). Beneficiary participation in development projects: empirical tests of popular theories, Economic Development and Cultural Change, Chicago: the University of Chicago.

(g) Other costs

Each national programme will have additional cost elements depending on the government 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).

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 achieved through 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 the different interventions used in the national programme.

New methods and improvements in existing methods can be more effectively evaluated for operational use when their economic benefits or limitations are fully understood. The benefits of such methods to dengue control programmes should be considered in the light of social and economic considerations as well as the impact of epidemics on health.

15. Strategic Plan for the Prevention and Control of Dengue in the Asia-Pacific Region: A Bi-regional Approach (2008–2015)

15.1 Need for a biregional approach and development of a Strategic Plan for the Prevention and Control of Dengue in the Asia-Pacific Region

Dengue is emerging rapidly as one of the major public health problems in countries of the Asia-Pacific Region, where nearly 1.8 billion people are estimated to be at risk against a global total of 2.5 billion. Epidemics of dengue are being reported more frequently and in an explosive manner. The disease continues to spread to new areas, including rural settings, in affected countries. Rapid spread of dengue in the Asia-Pacific Region is attributed to globalization, rapid unplanned and unregulated urban development, poor water storage and unsatisfactory sanitary conditions. Increased travel has contributed to the spread of viraemia.

In a region where ecological and epidemiological conditions are similar, effective control of dengue is not possible if the efforts are limited to one country or a few countries. Since dengue does not respect international boundaries, control efforts have to be coordinated regionally. In this direction, WHO took an initiative to develop a "Strategic Plan for the Prevention and Control of Dengue in the Asia-Pacific Region". Development of such a strategic plan is also important in meeting the requirements of the International Health Regulations (IHR) 2005.

Salient components of the Asia-Pacific Dengue Strategic Plan (2008–2015)[200] are outlined below.

15.2 Guiding principles

The Dengue Strategic Plan underlines several guiding principles intended for formulation, implementation and evaluation of activities in the prevention and control of dengue. The Strategic Plan:

- supports collaboration, cooperation and biregional solidarity for effective and sustained prevention and control of dengue in countries of the Asia-Pacific Region.
- uses existing policy frameworks and infrastructure as integral parts of dengue prevention and control programmes, and integrates disease surveillance within the umbrella of basic health services.
- uses national, multicountry, biregional and global partnerships to support country activities. The Strategic Plan will be harmonized within the Asia-Pacific Dengue Partnership (APDP).

- uses evidence-based interventions and best practices in developing and implementing dengue prevention and control programmes.
- uses networking to optimize available resources.
- supports intersectoral and interprogrammatic collaboration to maximize the provision of integrated services; e.g. developing links with the Asia-Pacific Strategy for Emerging Diseases (APSED) to strengthen health systems for surveillance and thereby contribute to IHR (2005).
- promotes the adoption of evidence-based interventions while at the same time recognizing the need for vaccine development, improved diagnostics and drugs and other innovations and intensifying related efforts.

15.3 Goal, vision and mission

The goal of the Strategic Plan is to reduce the disease burden due to major parasitic and vector-borne diseases to such an extent that they are no longer major public health problems.

The vision of the Strategic Plan is to minimize the health, economic and social impact of the disease by reversing the rising trend of dengue.

The mission of the Strategic Plan is to enhance the capacity in countries of the Asia-Pacific Region through partnerships so that evidence-based interventions can be applied in a sustainable manner through better planning, prediction and early detection, characterization and prompt control and containment of outbreaks and epidemics.

15.4 Objectives

The objectives are to enable Member countries to achieve the regional goal and realize the mission and vision of dengue prevention and control. Different countries will achieve these objectives and expected results in the context of their current capacities and policies.

General objective

- To reduce incidence rates of dengue fever and dengue haemorrhagic fever.

Specific objectives

- To increase the capacity of Member countries to monitor trends and reduce dengue transmission.
- To strengthen capacity to implement effective integrated vector management.
- To increase the health workers' capacity to diagnose and treat patients and improve health-seeking behaviour of communities.
- To promote collaboration among affected communities, national health agencies and major stakeholders to implement dengue programmes for behavioural change.
- To increase capacity to predict, detect early and respond to dengue outbreaks.
- To address programmatic issues and gaps that require new or improved tools for effective dengue prevention and control.

Expected results

The summary of expected results vis-à-vis objectives is given in Table 14.

Table 14: Summary of expected results related to objectives

S. No.	Objectives	Expected results
1	To increase the capacity of Member States to monitor trends and reduce dengue transmission.	1. Existing standard dengue case definition adopted. 2. Laboratory surveillance strengthened. 3. Regional dengue information system developed. 4. Mechanisms for sharing timely and accurate data strengthened. 5. Regional/intercountry response to timely advisory and resource (personnel, financial, stockpiling) mobilization improved. 6. Incorporate dengue surveillance (case, vector and seroprevalence) into an integrated and strengthened disease surveillance system. 7. Monitoring Member States' surveillance systems.
2	To strengthen capacity to implement effective integrated vector management.	1. Vectors fully described and vector indicators regularly monitored. 2. Regional IVM Strategy developed. 3. Evidence-based strategies to control vector populations adopted according to IVM principles. 4. Member State-level IVM strategy and guidelines developed. 5. Consistent with regional strategy. 6. Capacity to implement IVM, including training and recruitment of entomologists, strengthened. 7. Mechanisms to facilitate community involvement for vector control established. 8. Rational use of insecticides for vector control promoted. 9. Vector resistance monitoring strengthened.
3	To increase health workers' capacity to diagnose and treat patients and improve health-seeking behaviour of communities.	1. Public awareness increased on the warning signs and actions to be taken for dengue. 2. Strengthen capacity of health-care providers to diagnose, treat or refer cases. 3. Laboratory support for case management improved. 4. Referral network system in public and private sectors established.

S. No.	Objectives	Expected results
4	To promote collaboration among affected communities, national health agencies and major stakeholders to implement dengue programmes for behavioural change.	1. COMBI resource group for COMBI implementation established. 2. Assessment, including situation analysis of current strategies (social mobilization/health education) and extent and success of COMBI if implemented (with respect to dengue and other vector-borne diseases). 3. COMBI training implemented. 4. COMBI approach disseminated and promoted. 5. Development and implementation of COMBI plan supported. 6. Partnerships set up with private sector/and other multi-stakeholders.
5	To increase capacity to predict, detect early and respond to dengue outbreaks.	1. Early warning system/dengue surveillance system developed and scaled up. 2. Dengue outbreak standard operating system developed. 3. Coordination mechanisms within MoH and with other programmes and sectors established. 4. Intercountry coordination mechanisms in place. 5. A mechanism to incorporate rumour surveillance developed and implemented. 6. Regional outbreak response guidelines developed. 7. The ability of health workers to respond to the dengue outbreak strengthened. 8. Risk communication plan developed.
6	To address programmatic issues and gaps that require new or improved tools for effective dengue prevention and control.	1. Operational research capacity in dengue of existing academic/scientific institutions in Member States enhanced. 2. Disease burden estimated (epidemiological impact, social costs and cost of illness). 3. New knowledge gained, new tools developed, existing tools improved and new strategies created. 4. Evaluation of tools and strategies for dengue control and case management. 5. Translation of new improved tools into programmatic activities.

Source: World Health Organization. Asia-Pacific Dengue Strategic Plan (2008 – 2015). 2008. SEA/RC61/11 Inf. Doc. SEARO/WHO.[200]

15.5 Components of the Strategy

The following are the components of the strategy:

(1) Dengue surveillance.
(2) Integrated vector management.
(3) Case management.
(4) Social mobilization.
(5) Outbreak response communication.
(6) Research.

15.6 Supportive strategies

Dengue outbreaks/epidemics are a reflection of the failure of the public health system in a country to prevent and control dengue. Dengue is a neglected disease that becomes visible during an epidemic. Interest as well as commitment levels decline after the epidemic is controlled. Many of the affected countries do not even have a national programme for dengue. Its control requires a high level of sustained government and public interest and commitment, tangible strengthening of the public health infrastructure, intersectoral and intercountry collaboration, and community participation. A number of supportive strategies are needed for effective implementation of the Asia-Pacific Strategic Plan.

Supportive policy environment

A national policy should be prepared by the Ministry of Health in collaboration with other ministries and departments concerned. The policy should be the legal and regulatory framework which needs to ensure the health impact assessment of development projects related to industry and housing infrastructure and also appropriate designing of utilities such as evaporation (desert) coolers, water storage tanks, refrigerators and air-conditioners.

In addition, dengue should be made a notifiable disease, if not already, as mandated under the IHR (2005). The policy document should be endorsed by different stakeholders including the legislators. ***A healthy public policy[cd] includes the provision of health impact assessment of medium and large developmental projects that have the potential of encouraging breeding of the vector.*** The healthy public policy should contribute to effective vector control and reduce vector breeding.

Mobilization of resources

Despite the growing threat from dengue, resources for the control of dengue have not increased. National and international support continues to fall far short of the needs, even though there are untapped resources at the national, regional and global levels. To mobilize additional resources, synchronized action is needed with support from partners and different stakeholders. Harmonization of the strategy with the Asia-Pacific Dengue Partnership (APDP) is also required to mobilize the additional resources needed. Countries need to prepare operational plans that identify funding gaps. In addition, an advocacy plan should be prepared and implemented for mobilizing the resources on a sustained basis.

cd *Healthy public policies improve the conditions under which people live: secure, safe, adequate, and sustainable livelihoods, lifestyles, and environments, including housing, education, nutrition, information exchange, child care, transportation, and necessary community and personal social and health services. Policy adequacy may be measured by its impact on population health. http://www.searo.who.int/LinkFiles/Tools_&_Guidelines_SEA-MAL-255__Bookfold.pdf. Healthy public policy is characterized by an explicit concern for health and equity in all areas of policy and by accountability for health impact. http://www.who.int/healthpromotion/conferences/previous/adelaide/en/index1.html*

National dengue control programmes in Member countries should be implemented as part of national policy. These programmes have to find a niche and visibility within the existing disease surveillance programmes and the vector-borne disease control programme. It has to be a part of the basic health services and be able to find a place within the policy of decentralization in the national programme. Linkage to the IHR (2005) should also be encouraged.

Community participation

Dengue prevention and control efforts will be successful only if it becomes everyone's concern and responsibility. Sustained action is required at the individual, family and community levels. It has to be supported by the local self-government and the national government through the involvement of the health and other relevant sectors.[ce]

At the level of the individual and the family, self-reliant actions are needed for effective vector control and personal protection. This includes regular cleaning of containers in which water is stored, safe disposal of solid waste and prevention of vector breeding. Other responsibilities include monitoring vector activity within households and observing a weekly dry day. Vector breeding sites in the community include public places such as schools, places of worship, cinema halls, hospitals and community centres.

Besides supporting individuals and families, community actions can assist in monitoring and reducing vector breeding. Community groups can also work with industry that can help in dealing with the problem of used tyres, curing of plastic and cement water storage tanks and reducing the risk of vector breeding in refrigerators and water coolers. In addition, specific measures such as larviciding, insecticide spraying and biological control activities can be supported, subsequent to training and capacity-building.

For initiating and sustaining community participation, a strategic communication plan should be developed. Adoption of a COMBI strategy has demonstrated success in many countries. Best practices are recommended for documentation and adoption.[cf]

Partnerships

The Asia-Pacific Dengue Partnership (APDP) for Dengue Prevention and Control was formed in March 2006.[cg] At a meeting of the Core Group organized by the Regional Offices for the South-East Asia and Western Pacific Regions and the Government of Singapore held during February 2007 in Singapore, the Strategic Framework for the APDP was finalized. A biregional plan and a road map for the establishment of an executive board, secretaries and working groups were also agreed upon, in addition to all other relevant administrative matters.

The Asia-Pacific Strategic Plan for Dengue Prevention and Control recognizes that partnerships are required to strengthen collaboration between countries, establish networks within the country and across borders, enhance cooperation in access to innovations, and contribute to the discovery of improved tools. In addition, partnerships are crucial for mobilizing additional resources and showcasing the cause of dengue prevention and control through advocacy and sharing of quality knowledge on dengue widely.

ce For additional details, refer to Chapter 11.
cf For additional information, refer to Chapter 13.
cg WHO. Meeting of Partners on Dengue Prevention and Control in Asia-Pacific, Chiang Mai, Thailand, 23–24 March 2006 (SEA-VBC-91).

Programme planning and management

Effective programme management necessitates the preparation of an operational plan that identifies the resources committed and resource gaps. The capacity of staff at different levels – national, sub-national and district – in programme planning and management needs to be increased. Human resource development is a key component of capacity development. The development of capacity for the prevention and control of dengue is not an isolated effort but an integral part of strengthening the health system for improving the control of vector-borne diseases, disease surveillance and provision of basic health services.

Capacity development is to be undertaken based on training needs, the institutional environment and national policy. Since different countries in the Asia-Pacific Region have different health systems and policies, the dengue prevention and control programmes have to be consistent with the national situation. The Asia-Pacific Strategic Plan should be used by countries to develop/strengthen operational plans, including finding the best options.

Even within a decentralized or an integrated framework, it is necessary to identify the specific needs of dengue prevention and control so that control measures have adequate visibility. These include increased laboratory capacity, standard case management of dengue, and vector surveillance. Programme planning and management also includes developing a system for procurement, logistics and effective supply management. The health management information system and revamped surveillance are crucial in the context of dengue control since the disease often strikes in the form of outbreaks and epidemics.

15.7 Duration

The Strategic Plan is prepared to cover the period 2008–2015.

15.8 Monitoring and evaluation

A monitoring and evaluation framework is necessary to track the progress of implementation of the operational plan. M&E should be result-based and the framework should include outcome and output indicators that are easily measurable and verifiable. Some of the indicators that can be considered include the following:

- Number of countries that have a legal and regulatory framework for the prevention and control of dengue.
- Number of countries that allocate resources for the prevention and control of dengue.
- Number of national laboratories that are able to identify and characterize the virus.
- Reported dengue cases based on a three-year moving average.
- Proportion of outbreaks investigated within two weeks of first reporting.
- Case-fatality rates due to DHF/DSS.
- Number of countries that have developed and implemented IVM strategy.
- Number of countries that have COMBI plan developed and implemented.

15.9 Implementation of the Strategic Plan

Elements of the Strategic Plan overlap with those of the Asia-Pacific Partnership for Prevention and Control of Dengue in several areas. To implement the Plan, it would be necessary to harness the expertise available in the countries through collaboration and networking. Coordination will be achieved through the mechanism of the Regional Technical Advisory Groups and by forming a secretariat for the partnership. Technical guidance will also be the provided by the advisory group. It is proposed to develop a roadmap for the implementation of the strategy besides developing a log frame.

The first step after establishing a coordination mechanism will be to assist the countries in preparing operational plans with a budget, and identifying resource gaps and newer funding opportunities. Political, technical and managerial expertise in counties would need to be mobilized for increasing the capacity to implement the operational plans. Regular reviews[ch] of the programme should be encouraged and efforts made to promote research and innovations in the development of diagnostics, drugs and a vaccine for the prevention and control of dengue in the Asia-Pacific Region in addition to various operational aspects to improve the programme.

15.10 Endorsement of the Asia-Pacific Srategic Plan (2008–2015)

The Asia-Pacific Dengue Programme Manager's Meeting, which was held in Singapore in May 2008[ci] was attended by 17 Member countries from the WHO Western Pacific Region (WPR) and 5 from the South-East Asia Region. In addition, the meeting was attended by partner agencies and observers from ADB, UNEP, USAID and representatives from the health ministries of Japan and the Republic of Korea. The meeting facilitated the establishment and/or implementation of national plans.

While endorsing the Draft Asia-Pacific Strategic Plan 2008–2015, all 22 participating Member States worked on their respective national dengue control plans for the year 2009–2010. They also incorporated the requirements stipulated by the IHR 2005. Furthermore, countries without national programmes for dengue control were encouraged to involve the relevant ministries and other agencies for allocation of funds and ensure implementation of necessary activities. To start with, the programme managers planned for a two-year budget period and specified the funds to be provided by funding agencies.

ch For additional information, refer to the Guidelines for Conducting a Review of a National Dengue Prevention and Control Programme (WHO/CDS/CPE/PVC/2005.13).

ci Asia-Pacific Dengue Programme Managers Meeting in Singapore, May 5-9, 2008. Field Research Report. Asia-Pacific Dengue Programme Managers Meeting in Singapore, May 5-9, 2008. Prepared by Minako Jen Yoshikawa, 1 Kyoto University. http://www.cseas.kyoto-u.ac.jp/staff/nishibuchi/2008/doc/field_Resarch080505_en.pdf

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17. Annexes

1. Arbovirus laboratory request form

Name of patient _____ Hospital No. _____

Address _____ Hospital _____

Age _____ Sex _____ Physician _____

Date of admission _____ Admission complaint _____

Date of onset _____

Clinical findings:

1. Fever _____ °C or °F (max). Duration _____ days
2. Tourniquet test _____ Petechiae _____ Epistaxis _____
   Haematemesis/melaena _____ Other bleeding (describe) _____
3. Hepatomegaly _____ (cm at right costal margin). Tenderness _____
4. Shock _____ Blood pressure _____ (mmHg) Pulse _____ (per min.)
   Restlessness/Lethargy _____ Coldness of extremities/body _____

Clinical laboratory findings:

Platelets (X103) _____/mm^3 (on _____ day of illness)

Haematocrit (%) _____ (max) _____ (min)

Blood specimens

(Acute) Hospital admission	Hospital discharge	Convalescent
Date_____	Date_____	Date_____
○	○	○

Instructions: Fill the form completely with all clinical findings in duplicate. Saturate the filter-paper discs completely so that the reverse side is saturated and clip them to the form. Obtain admission and discharge specimens from all patients. If the patient does not return for a convalescent sample, mail promptly.

Source: *Dengue Haemorrhagic Fever: Diagnosis, treatment, prevention and control, Second edition, WHO, Geneva, 1995.*

2. International Health Regulations (IHR, 2005)

Core obligations for Member States

- Designate a National IHR Focal Point as the operational link for urgent communications concerning the implementation of the Regulations.
- Develop, strengthen and maintain the surveillance and response capacity to detect, assess, notify, report and respond to public health events, in accordance with the core capacity requirements under the IHR (2005).
- Notify WHO of all events that may constitute a public health emergency of international concern (PHEIC) within 24 hours of assessment by using the decision instrument [an algorithm].
- Respond to requests for verification of information regarding public health risks.
- Provide WHO with all relevant public health information, if a State Party has evidence of an unexpected or unusual public health event within it territory, which may constitute a PHEIC.
- Control urgent national public health risks that threaten to transmit diseases to other Member States.
- Provide routine inspection and control activities at international airports, ports and some ground crossings to prevent international disease transmission.
- Make every effort to fully implement WHO-recommended temporary and standing measures and provide scientific justification for any additional measures.
- Collaborate with other States Parties and with WHO in implementing the IHR (2005), particularly in the area of assessment, provision of technical and logistical support, and mobilization of financial resources.

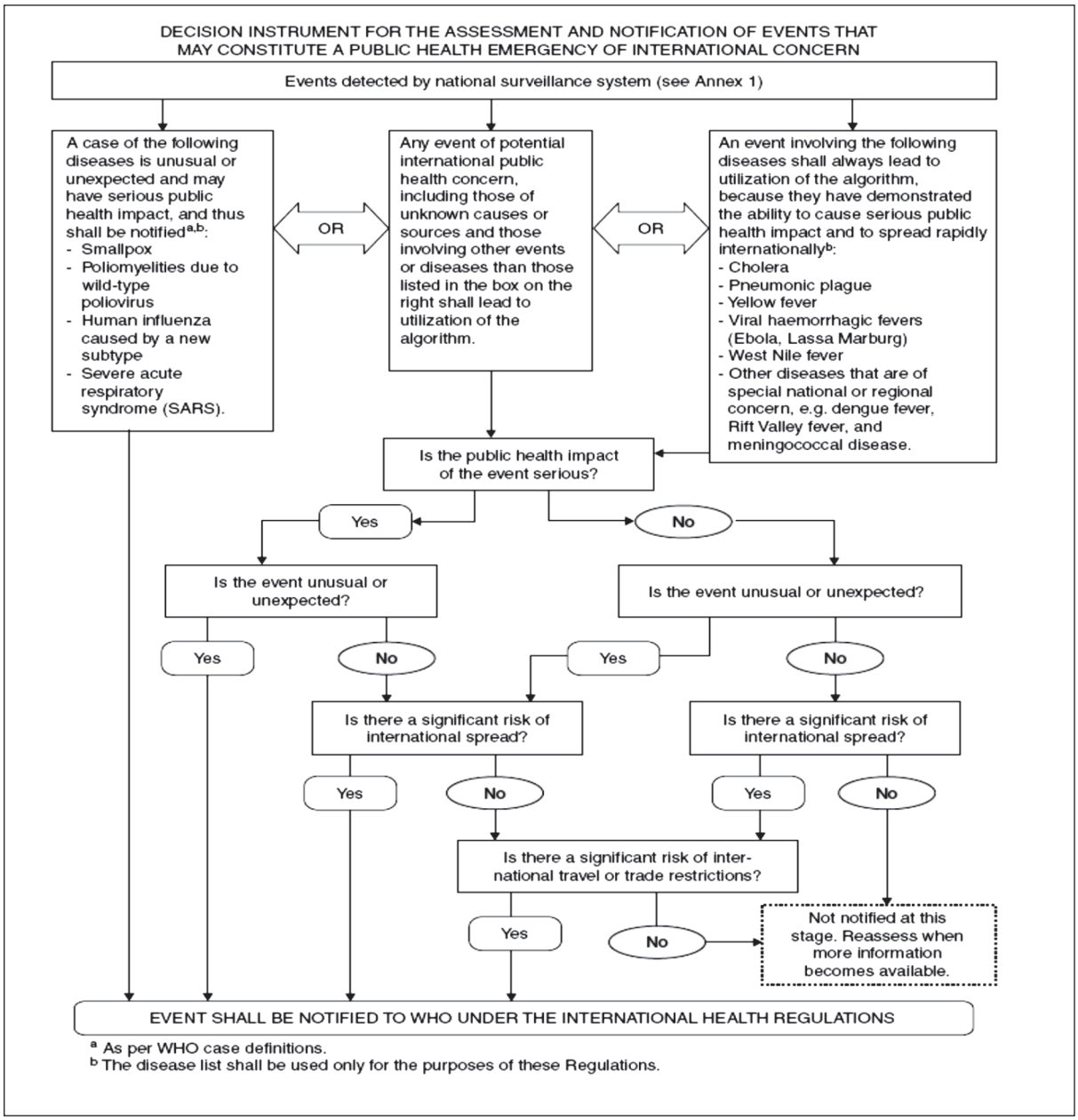
Core obligations for WHO

- Designate WHO IHR contact points as operational links for urgent communications concerning the implementation of the IHR (2005).
- Support Member States' efforts to develop, strengthen and maintain the core capacities for surveillance and response in accordance with the IHR (2005).
- Verify information and reports from sources other than official notifications or consultations, such as media reports and rumors, when necessary.
- Assess events notified by Member States (including on-site assessment, when necessary) and determine if they constitute a public health emergency of international concern.
- Provide technical assistance to States in their response to public health emergencies of international concern.
- Provide guidance to States to strengthen existing surveillance and response capacities to contain and control public health risks and emergencies.

- Provide all Member States with public health information to enable Member States to respond to a public health risk.
- Issue temporary and standing recommendations on control measures in accordance with the criteria and the procedures set out under the Regulations.
- Respond to the needs of Member States regarding the interpretation and implementation of the IHR (2005).
- Collaborate and coordinate its activities with other competent intergovernmental organizations or international bodies in the implementation of the IHR (2005).
- Update the Regulations and supporting guides as necessary to maintain scientific and regulatory validity.

Source: *http://www.who.int/ihr/about/en/ and http://www.who.int/ihr/about/FAQ2009.pdf*

3. IHR Decision Instrument for assessment and notification of events



Source: http://www.who.int/ihr/en/

4. Sample size in *Aedes* larval surveys

For *Aedes* larval surveys, the number of houses to be inspected in each locality depends on the level of precision required, level of infestation, and available resources. Although increasing the number of houses inspected leads to greater precision, it is usually impractical to inspect a large percentage of houses because of limited human resources.

Table A shows the number of houses that should be inspected to detect the presence or absence of infestation. For example, in a locality with 5000 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 A: 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
1000	258	138	57
2000	277	143	58
5000	290	147	59
10 000	294	148	59
Infinite	299	149	59

Table B shows the number of houses that should be inspected in a large (>5000 houses) positive locality, as determined by the expected House Index and the degree of precision desired. For example, if the preliminary sampling has indicated that the expected House Index is approximately 10%, and a 95% confidence interval of 8%–12% is desired, then 1000 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 a 5% chance that the true House Index is less than 6% or greater than 14%.

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 B). However, as seen in Table C, if the locality consists of only 1000 houses, the same precision will be obtained by inspecting 231 houses.

Table B: Precision of the *Aedes* House Index in large localities (>5000 houses)

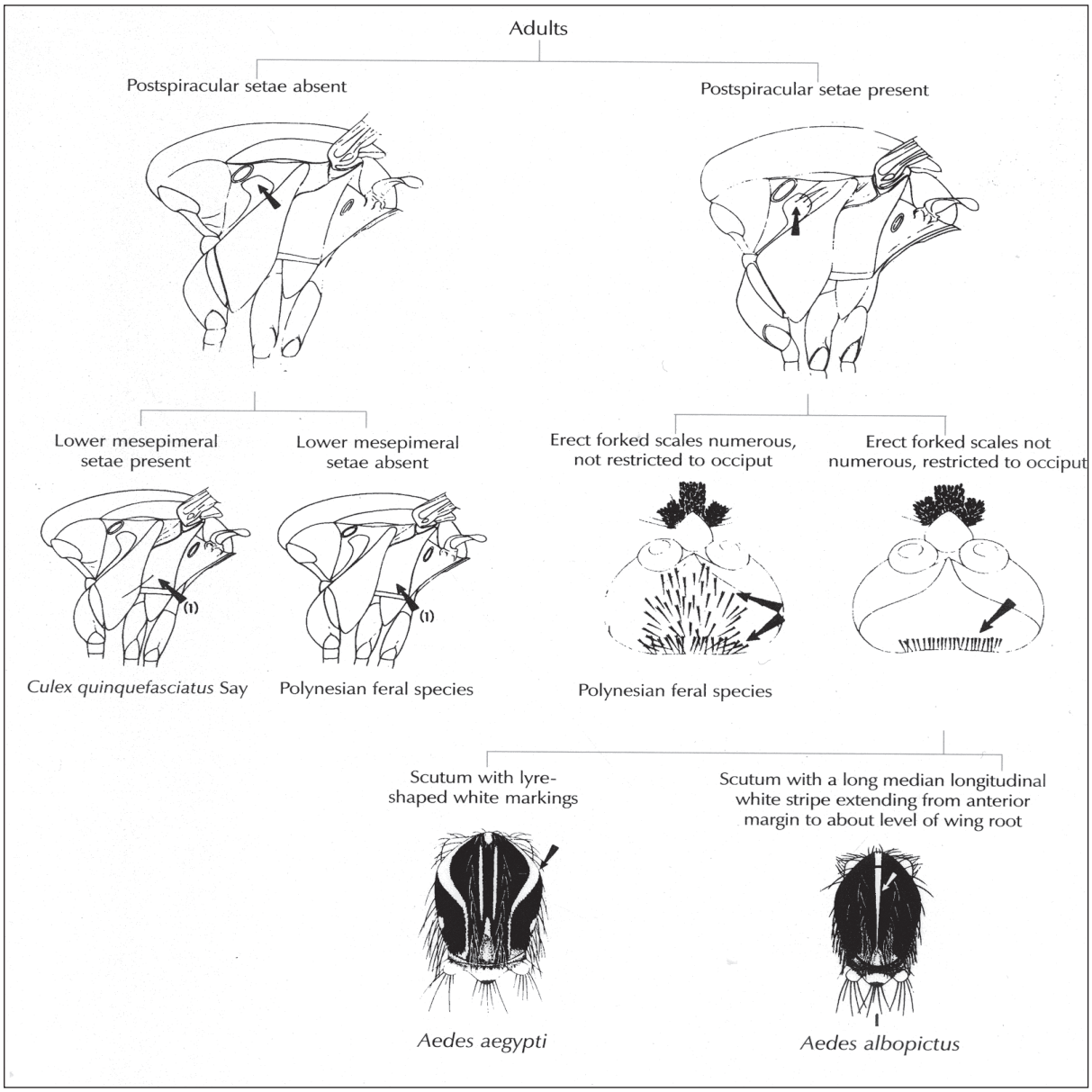
House Index (%)	95% confidence interval of the House Index Number of houses inspected			
	100	200	300	1000
2	0.2–7.0	0.5–5.0	0.7–4.3	1.2–3.1
5	2–11	2–9	3–8	4–7
10	5–18	6–14	7–14	8–12
20	13–29	16–26	16–25	18–23
50	40–60	43–57	44–56	47–53
70	60–79	62–76	64–75	67–73

Table C: 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 small locality (from Table B)			
	100	200	300	1000
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
1000	91	166	231	500
5000	100	200	285	830
10 000	100	200	300	910
20 000	100	200	300	950
30 000	100	200	300	1000
40 000	100	200	300	1000
100 000		200	300	1000

Source: Pan American Health Organization. Dengue and dengue haemorrhagic fever in the Americas: Guidelines for prevention and control. Washington: WHO/PAHO; 1994. (Scientific publication; no. 548).

5. Pictorial key to *Aedes (Stegomyia)* mosquitoes in domestic containers in South-East Asia

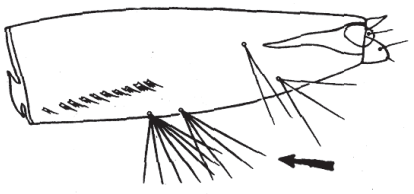


Source: Adapted from: Yiau-Min Huang. The mosquitoes of Polynesia with a pictorial key to some species associated with filariasis and/or dengue fever. Mosquito Systematics, 1977, 9(3): 289-322.

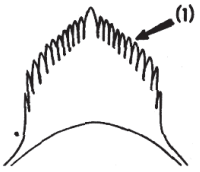
Annex 5 (contd)

Larvae

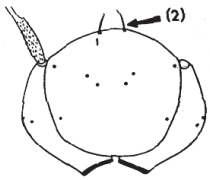
Siphon with 4 pairs of subventral tufts



(1) Mental plate with at least 10 teeth on each side of median tooth

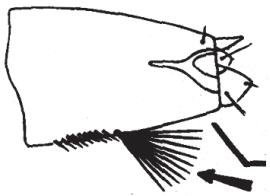


(2) Seta 1-C very slender, filamentous distally, usually very lightly pigmented

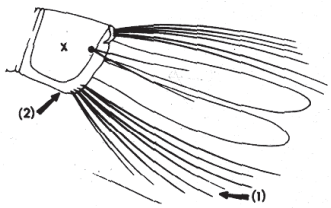


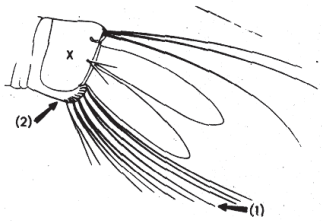
Culex quinquefasciatus Say

Siphon with a single pair of subventral tufts

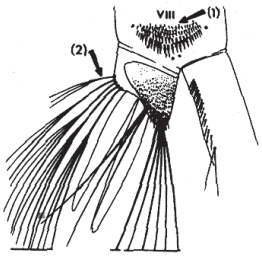


(1) Ventral brush with 4 or 5 pairs of setae and
(2) no precratal tufts



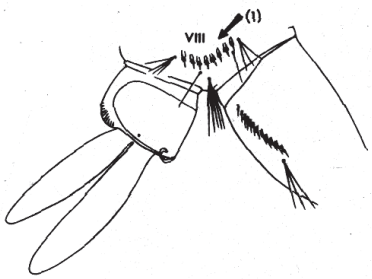


(1) Comb in a patch of several rows of scales, those of distal row elongate and varied in development

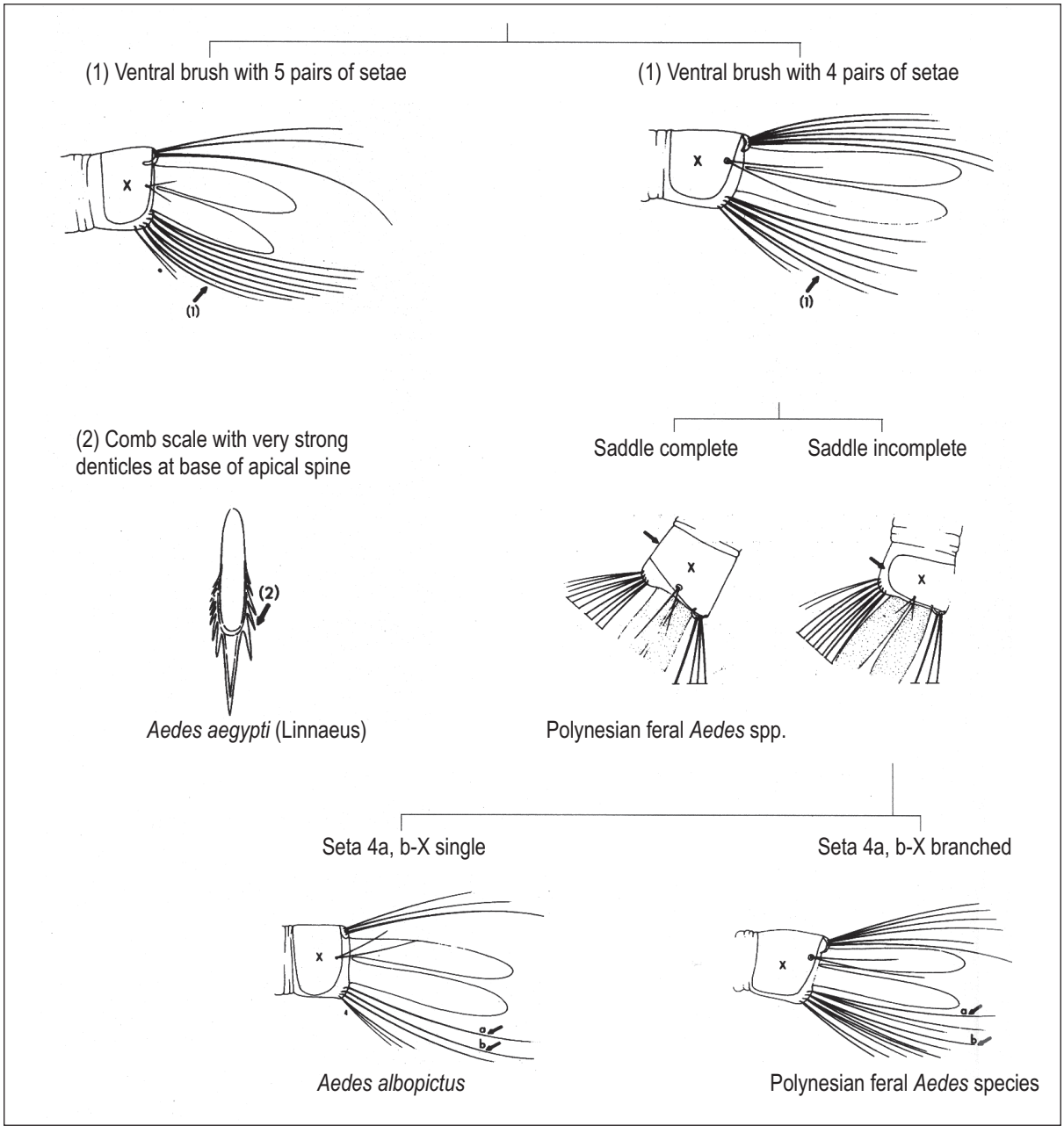


Polynesian feral *Aedes* species

(1) Comb in a single row

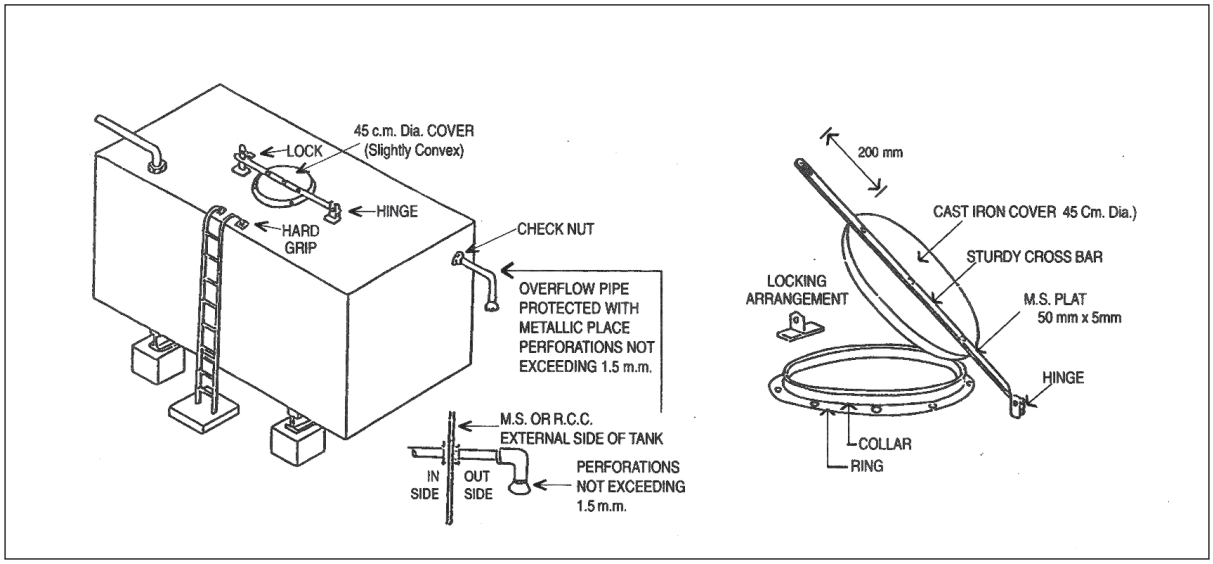


Annex 5 (contd)

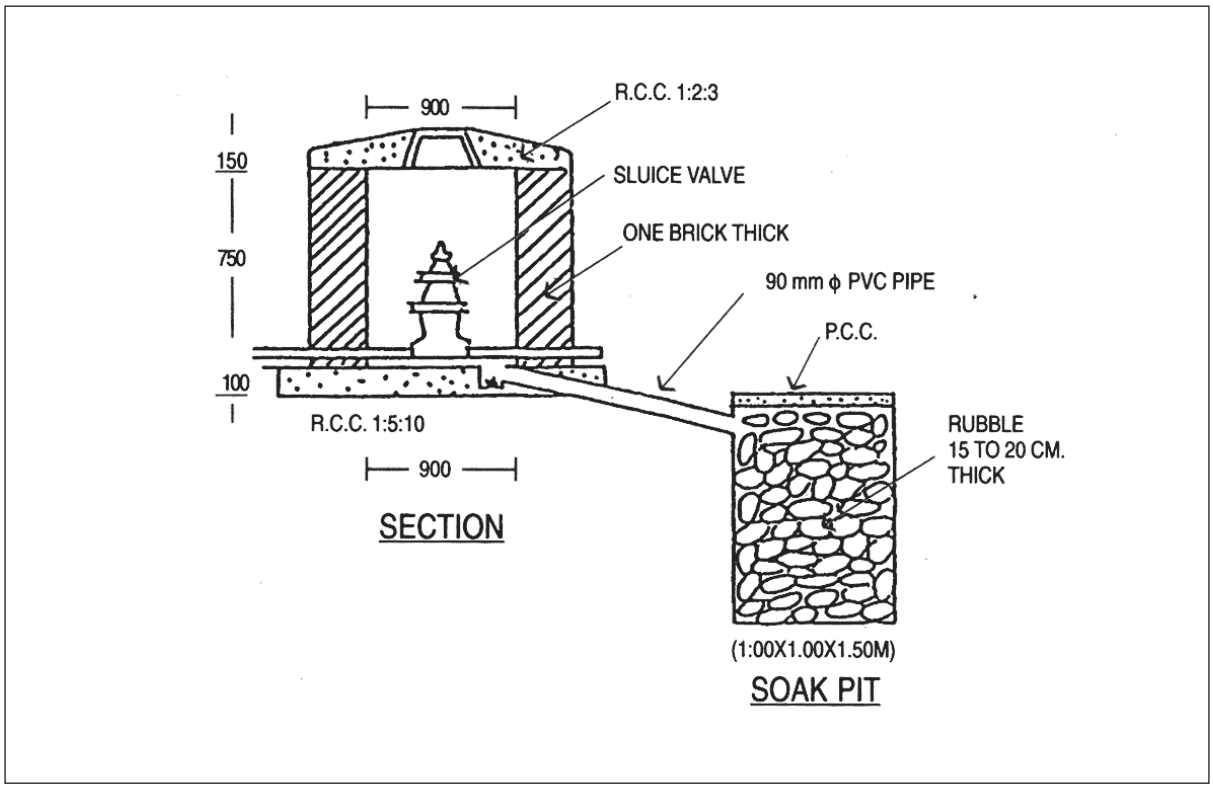


6. Designs for overhead tank with cover, masonry chamber and soak pit

(a) Standard design for overhead tank with cover design for mosquito proofing of overhead tanks and cisterns



(b) Design for masonry chamber and soak pit for sluice valve and water meter



Source: Sharma R.S., Sharma G.K., Dhillon GPS, Epidemiology and control of malaria in India. 1996. Dte. of NMEP, 22 Shamnath Marg, Delhi 110 054, India.

7. Procedure for treating mosquito nets and curtains

The steps described below mainly refer to treatment of mosquito nets with permethrin. The net treatment technique can be easily used for curtains.

(a) Calculate the area to be treated

Measure the height, length and width of the net. Assuming a rectangular mosquito net is 150 cm high, 200 cm long and 107 cm wide, the calculations are as follows:

Area of one end = 107 x 150 = 16 050 cm^2

Area of one side = 200 x 150 = 30 000 cm^2

Area of top = 107 x 200 = 21 400 cm^2

The sides and ends need to be multiplied by 2:

2 (16 050 + 30 000) = 92 100 + 21 400 = 113 500 cm^2

(end) (side) (top)

If 10 000 cm^2 = 1 m^2 then

113 500/10 000 = 11.35 m^2 area of net

(b) Determine how much insecticide is needed

Assume that a permethrin emulsifiable concentrate will be used, and the dosage desired is 0.5 grams per square metre.

To determine the total grams required, multiply the net size by the dosage:

11.35 x 0.5 = 5.67 grams of insecticide needed.

(c) Determine the amount of liquid required to saturate a net

In order to determine the percentage solution to be used for dipping, it is first necessary to determine the approximate amount of water retained by a net. Another term for dipping is soaking.

Pour five litres of water, but preferably a dilute solution of the insecticide to be used, into a plastic pan or other suitable container. For cotton, a 0.3% solution can be tried; for polyethylene or other synthetic fibre, a 1.5% solution can be tried. Add the net to the solution till it is thoroughly wet and then remove it. Allow the drips to fall into a bucket for 15 to 30 seconds. Set the net aside. Repeat the process with two other nets. Cotton nets can be lightly squeezed but not the synthetic ones. Measure the water or solution remaining in the dripping/soaking container and in the bucket to calculate the amount of liquid used per net.

Assuming that one polyethylene net retained 280 ml of solution, the percentage concentration required for dipping is calculated as follows:

$$\frac{\text{grams required per net}}{\text{ml solution retained per net}} = \frac{5.67}{280} = 2\%$$

(d) Preparation of dipping solutions to treat bulk quantities of mosquito nets or curtains

The general formula is:

$X = (A/B) - 1$

in which,

X = parts of water to be added to one part of emulsifiable concentrate.
A = concentration of the emulsifiable concentrate (%).
B = required concentration of the final solution (%).

Example: A 2.0% solution of permethrin for dipping nylon mosquito nets or curtains is to be prepared from a 25% concentrate.

$X = (25/2.0) - 1 = 12.5 - 1 = 11.5$

Therefore 11.5 parts of water to one part of concentrate are required, or one litre of concentrate to 11.5 litres of water.

Example: A 2.0% solution of permethrin for dipping nylon mosquito nets or curtains is to be prepared from a 50% concentrate.

$X = (50/2.0) - 1 = 24$

Therefore, 24 parts of water to one part of concentrate are required, or one litre of concentrate to 24 litres of water.

Example: A 0.3% solution of permethrin for dipping cotton mosquito nets or curtains is to be prepared from a 25% concentrate.

$X = (25/0.3) - 1 = 83.3 - 1 = 82.3$ or rounded to 82.

Therefore, 82 parts of water to one part concentrate are required, or one litre of concentrate to 82 litres of water, or half a litre of concentrate to 41 litres of water to accommodate a smaller container.

Example: A 0.3% solution of permethrin for dipping cotton mosquito nets or curtains is to be prepared from a 50% concentrate.

$X = (50/0.3) - 1 = 166.6 - 1 = 165.6$ or rounded to 166.

Therefore, 166 parts of water to one part of concentrate are required, or one litre of concentrate to 166 litres of water, or half a litre of concentrate to 83 litres of water to accommodate a smaller container.

(e) Preparation of a 2% dipping solution using a one litre bottle of 25% or 50% permethrin emulsifiable concentrate for soaking polyethylene or other synthetic fibre nets or curtains. This operational approach minimizes detailed measurements in the field.

For 25% concentrate:

Add 11.5 litres water to a container (with premeasured marks to indicate volume).

Add 1 litre (1 bottle) concentrate to the container.

Total volume: 12.5 litres

Grams permethrin: 250

% concentration: 2%

For 50% concentrate:

Add 24 litres water to a container.

Add one litre (one bottle) concentrate to the container.

Total volume: 25 litres

Grams permethrin: 500

% concentration: 2%

(f) Preparation of a 0.3% dipping solution using a one litre bottle of 25% or 50% permethrin emulsifiable concentrate for soaking cotton nets or curtains

For 25% concentrate:

Add 82 litres of water to a container.

Add one litre (one bottle) concentrate to the container.

Total volume: 83 litres

Grams permethrin: 250

% concentration: 0.3%

For 50% concentrate:

Add 166 litres of water to a container.

Add one litre (one bottle) concentrate to the container.

Total volume: 167 litres

Grams permethrin: 500

% concentration: 0.3%

(g) Drying of nets

Polyethylene and synthetic nets are dried in a horizontal position. Do not hang to dry. Drying the nets on mats removed from houses has proved to be convenient and acceptable. The nets should be turned over about once every hour for up to three or four hours. If the weather is good, the nets can be dried outside in the sun but for not more than several hours. Under rainy conditions, they can be placed in sheltered areas or inside and left overnight to dry. When dripping stops, they can be hung for completion of drying. Treated cotton nets which are not oversaturated and do not drip can be hung up to dry soon after the soaking procedure.

(h) Treatment of one net in a plastic bag (soaking)

As shown in (a) above, if it is assumed that the net size is 11.35 m^2, 5.67 grams of permethrin are needed to achieve a target dosage of 0.5 grams per square metre, and a net of this size absorbs 280 ml of solution.

The amount of 25% permethrin emulsifiable concentrate to use is determined as follows:

grams required x 100 = 5.67 x 100 = 22.68 ml (rounded to 23 ml)
% concentrated used: 25

Therefore, 23 ml of 25% permethrin is mixed with 280 ml of water. The net is placed inside the bag and the solution added. The net and solution are mixed together, shaken and kneaded in the bag. The net is removed and dried on top of the bag or a mat as described in (g) above. The amount of water can be reduced by 23 ml if there is excess run-off after the net is removed from the bag.

(i) Summary of treatment procedures

The important points in the treatment are summarized as follows:

(1) Dipping is the preferred method of net treatment. A 2% solution is usually sufficient to achieve a target dosage of 0.5 grams per square metre of permethrin on polyethylene, polyester, nylon or other type of synthetic fibre net or curtain. The residual effect lasts for six months or more. A 2% solution can be prepared simply by pouring the contents of a one litre bottle of 25% permethrin emulsion concentrate into a container with 11.5 litres of water. With a 50% concentrate, one litre is poured into 24 litres of water. The container used can be marked to show one or both of these volume levels. A 0.3% solution is normally required for cotton material, which absorbs more liquid. Staff need to check on the dosage applied and refine the operation accordingly. With bamboo curtains or mats used over doors or windows, a higher dosage (1.0 gram per square metre) can be used.

(2) Dipping the nets in a permethrin solution is a fast and simple method for treating nets and curtains in urban or rural housing conditions. Community members can easily learn the technique required for follow-up treatment. A dish-pan type of plastic or aluminum container which holds 15 to 25 litres of solution has been found to be quite suitable. Normally, about one litre of solution can treat four to five double (10m^2)-sized polyethylene or polyester nets. When the nets are removed from the solution, they should be held to drip in a bucket for no more than one minute before being laid out to dry in a horizontal position. Straw mats removed from houses are quite suitable for drying the nets outside in the open air. With one dipping station, about 150 nets or curtains can be treated in two hours or less.

(3) About 100 treated double-sized nets or an equivalent area of curtain material can protect 250 persons. It is not reasonable to expect every person in a crowded household to sleep under a net. It is important that every house in a community or village has one or two treated nets to kill mosquitoes so as to reduce the vector density. When used in this manner, protection is provided to those who do not even sleep under the nets. Infants and small children can sleep under the nets during the day.

8. Quantities of 1% temephos (abate) sand granules required to treat different-sized water containers to kill mosquito larvae

Table D: Quantities of 1% temephos (abate) sand granules required to treat different-sized water containers

Size of water jar, drum or other container (in litres)	Grams of 1% granules required	Number of teaspoons required, assuming one teaspoon holds 5 grams
Less than 25	Less than 5	Pinch: small amount held between thumb and finger
50	5	1
100	10	2
200	20	4
250	25	5
500	50	10
1000	100	20

Methoprene (altosid) briquettes can also be used in large water drums or overhead storage tanks. One briquette is suitable to treat 284 litres of water. Briquettes of *Bacillus thuringiensis H-14* can also be used in large cistern tanks.

Source: WHO/Western Pacific Region Background Document No. 16, 1995.

9. Procedure, timing and frequency of thermal fogging and ULV space spray operations

Basic steps

The steps listed below are to be followed in carrying out the space spraying of a designated area:

- The street maps of the area to be sprayed must be studied carefully before the spraying operation begins.
- The area covered should be at least 300 metres within the radius of the house where the dengue case was located.
- Residents should be warned before the operation so that food is covered, fires extinguished and pets are moved out together with the occupants.
- Ensure proper traffic control when conducting outdoor thermal fogging since it can pose a traffic hazard to motorists and pedestrians.
- The most essential information about the operational area is the **wind direction.** Spraying should always be done from downwind to upwind, i.e. going against the direction of the wind.

Vehicle-mounted spraying

- Doors and windows of houses and buildings in the area to be sprayed should be opened.
- The vehicle is driven at a steady speed of 6–8 km/h (3.5–4.5 miles/h) along the streets. Spray production should be turned off when the vehicle is stationary.
- When possible, spraying should be carried out along streets that are at right angles to the wind direction. Spraying should commence on the downwind side of the target area and progressively move upwind.
- In areas where streets run parallel as well as perpendicular to the wind direction, spraying is only done when the vehicle travels upwind on the road parallel to the wind direction.
- In areas with wide streets with houses and buildings far away from the roadside, the spray head should point at an angle to the left side of the vehicle (in countries where driving is on the left side of the road). The vehicle should be driven close to the edge of the road.
- In areas where the roads are narrow, and houses are close to the roadside, the spray head should be pointed directly towards the back of the vehicle.
- In dead-end roads, the spraying is done only when the vehicle is coming out of the dead-end, not while going in.
- The spray head should be pointed at a 45° angle to the horizontal to achieve maximum effect with droplets.
- Vector mortality increases downwind as more streets are sprayed upwind in relation to the target area.

Portable thermal fogging

- Thermal fogging with portable thermal foggers is done from house to house, always fogging from downwind to upwind.
- All windows and doors should be shut for half an hour after the fogging to ensure good penetration of the fog and maximum destruction of the target mosquitoes.
- In single-storeyed houses, fogging can be done from the front door or through an open window without having to enter every room of the house. All bedroom doors should be left open to allow dispersal of the fog throughout the house.
- In multistoreyed buildings, fogging is carried out from upper floors to the ground floor and from the back of the building to the front. This ensures that the operator has good visibility along his spraying path.
- When fogging outdoors, it is important to direct the fog at all possible mosquito resting sites, including hedges, covered drains, bushes, and tree-shaded areas.
- The most effective type of thermal fog for mosquito control is a medium/dry fog, i.e. it should just moisten the hand when the hand is passed quickly through the fog at a distance of about 2.5–3.0 metres in front of the fog tube. Adjust the fog setting so that oily deposits on the floor and furniture are reduced.

Backpack aerosol spraying with ULV attachments

- Each spray squad consists of four spraymen and one supervisor.
- Each sprayman sprays for 15–30 minutes and is then relieved by the next sprayman. For reasons of safety, he must not spray when tired.
- The supervisor must keep each sprayman in his sight during actual spraying in case he falls or needs help for any reason.
- Do not directly spray humans, birds or animals that are in front of spray nozzles and less than five metres away.
- Spray at full throttle. For example, a ULV Fontan nozzle tip 0.4 can deliver 25 ml of malathion per minute, and a 0.5 tip, 65 ml. The smaller tip is usually preferred unless spraymen move quickly from house to house. Some machines can run for about one hour on a full tank of petrol.

House-spraying technique

- Do not enter the house. House spraying means spraying in the vicinity of the house.
- Stand 3–5 metres in front of the house and spray for 10 to 15 seconds directing the nozzle towards all open doors, windows and eaves. If appropriate, turn away from the house and, standing in the same place, spray the surrounding vegetation for 10 to 15 seconds.
- If it is not possible to stand three metres from the house due to the closeness of houses and lack of space, the spray nozzle should be directed towards house openings, narrow spaces and upwards.
- While walking from house to house, hold the nozzle upwards so that particles can drift through the area. Do not point the nozzle towards the ground.
- Spray particles drift through the area and into houses to kill mosquitoes which become irritated and fly into the particles. The settled deposits can be residual for several days to kill mosquitoes resting inside houses and on vegetation not exposed to the rain.

- This technique permits treatment of a house with an insecticide ranging from 1 gram to 25 grams in one minute. The dosage depends on the discharge rate, concentration of insecticide applied, and the time it takes to spray the house. For comparison, an indoor residual house spray may require 30 minutes of spraying to deposit 300 grams of insecticide. This assumes a dosage of two grams per square metre to 150 square metres of sprayable surface.

Information to be given to inhabitants

- Time of spraying, for example, 0630 to 1000 hours.
- All doors and windows should be open.
- Dishes, food, fish tanks and bird cages should be covered.
- Stay away from open doors and windows during spraying, or temporarily leave the house and/or the sprayed area until the spraying is completed.
- Children or adults should not follow the spray squad from house to house.

Timing of application

Spraying is carried out only when the right weather conditions are present and usually only at the prescribed time. These conditions are summarized below:

For optimum spraying conditions (Table E), please note the following:

- In the early morning and late evening hours, the temperature is usually cool. Cool weather is more comfortable for workers wearing protective clothing. Also, adult *Aedes* mosquitoes are most active at these hours.
- In the middle of the day, when the temperature is high, convection currents from the ground will prevent concentration of the spray close to the ground where adult mosquitoes are flying or resting, thus rendering the spray ineffective.
- An optimum wind speed of between 3 km/h and 13 km/h enables the spray to move slowly and steadily over the ground, allowing for maximum exposure of mosquitoes to the spray. Air movements of less than 3 km/h may result in vertical mixing while winds greater than 13 km/h disperse the spray too quickly.
- In heavy rain, the spray generated loses its consistency and effectiveness. When the rain is heavy, spraying should stop and the spray head of the ULV machine should be turned down to prevent water from entering the blower.
- Spraying is permissible during light showers. Also, mosquito activity increases when the relative humidity reaches 90, especially during light showers.

Table E: Conditions for spraying

	Most favourable conditions	Average conditions	Unfavourable conditions
Time	Early morning (0630–0830 hrs) or late evening	Early to mid-morning or late afternoon, early evening	Mid-morning to mid-afternoon
Wind	Steady, between 3–13 km/h	0–3 km/h	Medium to strong, over 13 km/h
Rain	No rain	Light showers	Heavy rain
Temperature	Cool	Mild	Hot

Frequency of application

The commencement and frequency of spraying generally recommended is as follows:

- Spraying is started in an area (residential houses, offices, factories, schools) as soon as possible after a DF/DHF case from that area is suspected.
- At least one treatment should be carried out within each breeding cycle of the mosquitoes (seven to ten days for *Aedes*). Therefore, a repeat spraying is carried out within seven to ten days after the first spraying. Also, the extrinsic incubation period of dengue virus in the mosquito is 8 to 10 days.

Evaluation of epidemic spraying

Within two days after spraying during outbreaks, a parous rate of 10% of female mosquito have already laided eggs or less, compared with a much higher rate before spraying, indicates that most of the mosquito population is newly emerged and incapable of transmitting the disease. This also indicates the spray was effective and had greatly reduced transmission by killing the older infected mosquito population.

However, a low parous rate after spraying can occur in the absence of a marked reduction in vector density. This can be attributed to the emergence of a new population of mosquitoes which escaped the spray, a relatively low adult density before spraying and adult sampling methods which show considerable variations in density in the absence of control. An effective spray programme should also be accompanied by a reduction in hospitalized cases after the incubation period of the disease in humans (about 5–7 days) has elapsed. The spraying should be repeated at seven-day intervals to eliminate the possibility of infected mosquitoes.

Source: WHO Western Pacific Region Background Document No.16, 1995.

10. Safety measures for insecticide use

Safety measures for insecticide use are adopted to protect the health and lives of those applying insecticides. These measures seek to minimize the degree of poisoning by insecticides and exposure to insecticides, prevent accidental poisoning, monitor sub-acute poisoning, and provide adequate treatment for acute poisoning. These measures can be broken down into the four broad categories listed below.

Four issues for safety measures:

- the choice of insecticides to be used;
- the safe use of insecticides;
- the monitoring of sub-acute insecticide poisoning; and
- the treatment of insecticide poisoning.

The human population exposed to insecticide treatment is of prime importance. It must be ensured that they are not exposed to health hazards.

1. Choice of insecticides to be used

The choice of an insecticide for vector control is determined by the following factors:

- toxicity and its safety to humans and the environment;
- effectiveness against the vector; and
- cost of the insecticide.

In weighing the relative importance of the three factors above, the following are important aspects from a safety standpoint:

- An effective and/or cheap insecticide should not be used if the chemical is highly toxic to humans and other non-target organisms.
- Pyrethroids, generally, have very low mammalian toxicity when compared with other groups of insecticides such as carbamates.
- The liquid formulation of an insecticide is usually more dangerous than a solid formulation of the same strength. Certain solvents in liquid formulation facilitate skin penetration.
- With regard to occupational exposure, dermal exposure is more important than gastrointestinal or respiratory exposure. Thus, an insecticide with low dermal toxicity is preferred.
- The latest information on the safety aspect of insecticides being considered must be available before a wise choice can be made.

2. The safe use of insecticides

The key to the safe use of insecticides is to control and minimize the level of routine or accidental exposure of an individual to a given insecticide. The level of exposure is in turn dependent on many factors, as outlined in the box below.

Level of exposure depends on:

- Insecticide storage conditions.
- Personal hygiene and attitude of workers.
- Knowledge and understanding of workers concerning insecticides.
- Equipment used.
- Method and rate of application.
- Environmental conditions such as prevailing winds, temperature and humidity.
- Duration of the work.
- Protective clothing and mask used.

In order to minimize the routine and accidental exposure of staff to insecticides, safety precautions must be observed at all stages of insecticide use.

Safety precautions during storage

- Store insecticides in containers with the original label. Labels should identify the contents, nature of the material, preparation methods and precautions to be employed.
- Do not transfer insecticides to other containers, or to containers used for food or beverages.
- All insecticide containers must be sealed.
- Keep insecticides in a properly-designated place, away from direct sunlight, food, medicine, clothing, children and animals and protected from rain and flooding, preferably in a locked room with warning signs such as "Dangerous: Insecticides; Keep Away" posted prominently.
- To avoid unnecessary and prolonged storage of insecticides, order only sufficient amounts needed for a given operation, or order on a regular basis (e.g. every three months depending on routine needs), or order only when stocks get low.
- Stocks received first must be used first. This avoids prolonged storage of any batch of insecticide.

Steps before insecticide use

- Read the label carefully and understand the directions for preparing and applying the insecticides as well as the precautions listed, then follow the precise directions and precautions.
- Know the first-aid measures relevant and antidotes for the insecticides being used.

During mixing and spraying/fogging with insecticides

- Do not drink, eat or smoke while working. This prevents accidental inhalation or ingestion of insecticides.
- Mix insecticides in a well ventilated area, preferably outdoors.

- Mix only as much insecticide as is needed for each application. This will reduce the problem of storing and disposing of excess insecticide.
- Do not smell or inhale insecticides.
- Never mix insecticides directly with bare hands.
- Stand with the wind blowing from behind when mixing insecticides.
- Do not clear blocked spray nozzles by blowing with the mouth.
- Make sure that the spray equipment does not leak; check all joints regularly.
- Keep all persons not involved away from where the insecticides are being mixed.
- Exposure to spraying normally should not exceed five hours a day.
- When spraying is undertaken, the hottest and most humid period of the day should be avoided if possible. It is best to apply insecticides early in the morning or late in the evening. This minimizes excessive sweating and encourages the use of protective clothing. Also, high temperatures increase the absorption of insecticides.
- Those applying insecticides should always wear long-sleeved shirts and trousers.
- Wear protective clothing and headgear, where necessary, to protect the main parts of the body as well as the head and neck, lower legs, hands, mouth, nose and eyes. Depending on the insecticide and type of application, boots, gloves, goggles and respirators may be required.
- Mixers and baggers should wear rubber boots, gloves, aprons and masks, since they come in contact with technical material and concentrated formulations.
- Those engaged in thermal fogging and ULV spraying should be provided with overalls, goggles, hats and masks.
- Those engaged in larviciding (e.g. with temephos) need no special protective clothing because the risk of toxicity is low.
- To protect yourself and your family, never work with insecticides in your street clothes.
- Do not wear unwashed protective clothing. Make sure your gloves and boots have been washed inside and outside before you put them on.
- Take heed of the wind direction to avoid drift.

Steps after spraying/fogging of insecticides

- Wash all spray equipment thoroughly and return to the storeroom. It is important to maintain equipment in good working order after usage.
- Empty insecticide containers should not be used in the household to store food or drinking water. They should be buried or burned. Larger metal containers should be punctured so that they cannot be reused.
- Used containers can be rinsed two or three times with water, scrubbing the sides thoroughly. If a drum has contained an organophosphorus compound, an additional rinse should be carried out with washing soda, 50 g/l (5%), and the solution should be allowed to remain in the container overnight. A soakage pit should be provided for rinsing.
- All workers must wash thoroughly with soap and water. This removes deposits of insecticides on the skin.
- All protective clothing should be washed after each use.
- All use of insecticides must be recorded.
- Eat only after thoroughly washing hands with soap and water.

3. Monitoring sub-acute insecticide poisoning

Regular medical surveillance of all spraying personnel may be required if space spray operations are done on a routine, long-term basis.

- Mixers, baggers and spraymen should be instructed to detect and report any early signs and symptoms of mild intoxication.
- Any undue prevalence of illness not associated with well recognized signs and symptoms of poisoning by a particular insecticide should be noted and reported.
- A regular medical examination, including the determination of blood cholinesterase for those applying organophosphorus compounds, should be conducted. If the level of cholinesterase activity decreases significantly (50% of a well-established pre-exposure value), the affected operator must be withdrawn from exposure until he recovers. Test kits for monitoring cholinesterase activity are available.

Symptoms of insecticide poisoning

Field workers should be taught to recognize the following symptoms:

DDT and other organochlorines

Symptoms include apprehension, excitement, dizziness, hyperexcitability, disorientation, headache, muscular weakness and convulsions . These compounds are normally not used for DHF vector control.

Malathion, fenitrothion and other organophosphates

Early symptoms include nausea, headache, excessive sweating, blurred vision, lacrimation (tears from eyes), giddiness, hypersalivation, muscular weakness, excessive bronchial secretion, vomiting, stomach pains, slurred speech and muscular twitching. Later, advanced symptoms may include diarrhoea, convulsions, coma, loss of reflexes, and loss of sphincter control.

(Note: Temephos has a very low toxicity rating and can safely be used in drinking water to kill mosquito larvae).

Carbamates

Symptoms include headache, nausea, vomiting, bradycardia, diarrhoea, tremors, convulsive seizures of muscles, increased secretion of bronchial, lacrimal, salivary and sweat glands .

Pyrethroids (e.g. permethrin and S-bioallethrin)

These insecticides have very low mammalian toxicity, and it is deduced that only single doses above 15 gm could be a serious hazard to an adult. In general, the effective dosages of pyrethroids for vector control are much lower when compared with other major groups of synthetic insecticides. Although pyrethroids may be absorbed by ingestion, significant skin penetration is unlikely. Symptoms, if they develop, reflect stimulation of the central nervous system. No cases of accidental poisoning from pyrethroids have been reported in humans. Some pyrethroids such as deltamethrin, cypermethrin and lambdacyhalothrin, can cause eye and skin irritation if adequate precautions are not taken.

Bacterial insecticide bacillus thuringiensis H-14 and insect growth regulators (methoprene)

These control agents have exceedingly low mammalian toxicity and cause no side-effects. They can be safely used in drinking water.

4. Treatment of acute insecticide poisoning

- Know the symptoms of poisoning due to different insecticides.
- Call a physician.
- Begin emergency treatment in the field. This treatment is continued during transport and ends in a medical centre.
- Provide supportive treatment for the patient. This may include:
  - Artificial respiration if spontaneous respiration is inadequate.
  - A free airway must be maintained. Excess vomitus and secretions should be removed.
  - Oxygen therapy for cyanosis (a blue or purplish discolouration of the skin due to insufficient oxygen).
- Decontaminate the patient as soon as possible. This may involve:
  - Removal of contaminated clothing.
  - Thorough washing of the skin and hair with soap and water.
  - Flushing contaminated eyes with water or saline solution for 10 minutes.
  - Evacuation to fresh air.
- Eliminate the poison. Determine whether the insecticide is in water emulsion or petroleum solution, if possible.
  - If the insecticide is dissolved in a water emulsion, induce vomiting by putting a finger or spoon down the throat. If this fails, give one tablespoon of salt in a glass of warm water until vomitus is clear.
  - If the insecticide is dissolved in a petroleum product, have the doctor or nurse perform gastric lavage, sucking the insecticide out of the stomach with a tube to prevent the possibility of the petroleum product entering the lungs and causing pneumonia.
  - Administer a laxative such as Epsom salts or milk of magnesia in water to eliminate the insecticide from the alimentary tract. Avoid oily laxatives such as castor oil, which may increase the absorption of insecticide.
- Administer an antidote where possible. This involves the following steps:
  - The insecticide container must be made available to the physician wherever possible. This will help in determining the group of insecticides involved in the poisoning. The label will indicate if it is a chlorinated hydrocarbon, an organophosphate, a carbamate, a pyrethroid or a bacterial insecticide.
  - If the insecticide is an organophosphate, either airopine sulphate or a 2-PAM chloride (pralidoxime chloride) can be used as an antidote. An injection of 2 mg to 4 mg atropine sulfate is given intravenously. More atropine may be required depending on the severity of the poisoning. The dose of 2-PAM chloride is 1 gram for an adult and 0.25 gram for an infant.
  - If the insecticide is a carbamate, atropine sulphate is used as an antidote; 2-PAM and other oximes are not to be used.

Source: WHO Western Pacific Region. Background Document No.16, 1995

11. Functions of Emergency Action Committee (EAC) and Rapid Action Team (RAT)

(A) Emergency Action Committee (EAC)

Constitution

The EAC will comprise administrators, epidemiologists, entomologists, clinicians and laboratory specialists, school health officers, health educators and representatives of other related sectors.

Functions

(1) To take all administrative actions and coordinate activities aimed at the management of serious cases in all medical care centres and undertake emergency vector control intervention measures.

(2) To draw urgent plans of action and resource mobilization in respect of medicines, intravenous fluids, blood products, insecticides, equipment and vehicles.

(3) To liaise with intersectoral committees in order to mobilize resources from non-health sectors, namely the ministry/department of - urban development, education, information, law, water supply, waste disposal for the elimination of the breeding potential of *Aedes aegypti*.

(4) To interact with the news media and NGOs for dissemination of information related to health education and community participation.

(B) Rapid Action Team (RAT)

Constitution

The RAT at the state or provincial levels will comprise epidemiologists, entomologists and a laboratory specialist (at state and local levels).

Local levels

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

Functions

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

Source: Management of Dengue Epidemic, Report of a WHO Technical Meeting, New Delhi, 28–30 November 1996, WHO Regional Office for South-East Asia, New Delhi (SEA/DEN/1, SEA/VBC/55, May 1997, 38 pp).

12. Case Investigation Form (prototype)

ID no.:
Name of hospital/institution/clinic:
Locality/town/city:
Date:
Case investigation:
Name:
Age:
Sex:
Father's/mother's name:
Address:
Whether visited any other area during last two weeks:
Signs and symptoms:
Date of onset of fever:
Date of admission:
Course of fever: continuous/intermittent/remittent
Presenting symptoms:
Haemorrhagic manifestations: Yes/no
Petechiae, parpura, ecchymosis, epistaxis, gum bleeding, haematemesis, malena
Enlarged lever: Yes/no
Torniquet test: Positive/negative/not done
Rash: Yes/no
Shock: Yes/no
Condition of patient: stable/critical
Any platelet or blood transfusion given:
Laboratory findings:

Haematocrit (percentage)	Serial readings	1
		2
Platelet count	Serial readings	1
		2
Differential leucocyte count	Serial readings	1
		2
Seroogical input: NS1, IgM, IgG		
Acute sera collected on date:	Sent on date:	
Convalescent sera collected on date:	Sent on date:	
Outcome of the patient:	Recovered/expired/discharged on:	
		Signature (Medical Officer/ Designated authority)

Source: Adapted from Dengue Fever, Dengue Haemorrhagic Fever, Dengue Shock Syndrome Investigation Guidelines. Version 01/2010. Kansas, USA

Dengue fever (DF) is the fastest emerging arboviral infection spread by *Aedes aegypti* mosquitoes with major public health consequences for millions of people around the world, and in particular the South-East Asia and Asia-Pacific Regions of the World Health Organization (WHO). Of the 2.5 billion people globally at risk of DF and its severe forms dengue haemorrhagic fever (DHF) and dengue shock syndrome (DSS) South-East Asia accounts for approximately 1.3 billion or 52%.

As the disease spreads to new geographical areas, the frequency of the outbreaks has increased along with a rapidly changing disease epidemiology. In response to resolution of the Forty-sixth World Health Assembly urging Member States to strengthen national programmes for control of DF/DHF, several documents were developed by regional offices of WHO, including South-East Asia.

In 1999 the WHO Regional Office for South-East Asia published the *Regional Guidelines for the Prevention and Control of DF/DHF.* Since then new strategies and developments in the control of dengue fever, DHF and DSS have come to light. *The Regional Guidelines* were extensively revised, updated and expanded with the focus on new and additional topics of current relevance to the populations of Member States of the Region. They were then rechristened the *Comprehensive Guidelines for the Prevention and Control of Dengue and Dengue Haemmorhagic Fever.*

This revised and expanded edition of the *Comprehensive Guidelines* is intended to provide guidance to national and local-level programme managers and public health officials of Member States, as well as other stakeholders, including health practitioners, laboratory personnel and multisectoral partners, on strategic planning, implementation, monitoring and evaluation, and strengthening the response to dengue prevention and control in their countries. Scientists and researchers involved in vaccine and antiviral drug development will also find crucial baseline information in this document.

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