Early Warning and Reporting System (EWARS) Guidelines

Government of Nepal
Ministry of Health
Department of Health Services
Epidemiology and Disease Control Division
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PREFACE

Disease surveillance is the collection of data for action. By collecting information about cases of the disease, and appropriately analyzing the data, we can determine what actions are needed to reduce morbidity, disability and mortality. Decisions on resources allocation and on the definition of priorities and objectives cannot be made without a data base in order to identify problems and their pattern of distribution in the population.

Following WHO Global and regional call for the implementation of a reliable reporting system capable of early detecting and monitoring new, emerging and/or reemerging diseases, Epidemiology and Disease Control Division of Department of Health Services has established an Early Warning Reporting System (EWARS).

In order to develop an active, timely and accurate sentinel surveillance reporting system, districts identified at high risk were provided with facilities for rapid dissemination of the information. This will be helpful not only to improve the timeliness of the reports to the central level and to facilitate the district analysis of their information, but also will provide the program managers immediate access to the necessary information produced by the districts to take appropriate actions. By doing this, the EWARS will allow the early detection of focal outbreaks of communicable and infectious diseases, which can lead to timely interventions for the control of these diseases.

For the initial phase in 1997, eight hospitals were selected as sentinel sites and six diseases were targeted for reporting. EDCD has further expanded the EWARS sentinel sites in 16 more hospitals in year 1998.Similarly it was expanded upto 26 sites in 2002, upto 28 sites in 2003 and upto 40 sites in 2008 and is reporting six targeted diseases/syndromes: Malaria, Kala-azar, Dengue fever, acute gastroenteritis, Cholera and Severe Acute Respiratory Infection. In each of these sites medical recorder were identified as focal person for the reporting cases (immediately and weekly).

In 2015, EWARS was identified in 81 sentinel sites and is currently operational in 51 sentinel sites covering 44 districts. Control room has been established under surveillance and research section (in technical support from WHO, NHSSP and GIZ) in order to maintain quality, accuracy, timeliness and completeness of data received from EWARS sentinel sites. Similarly EWARS bulletin is produced on every Sunday and shared it to all concerned persons and stakeholders via email. In order to maintain the quality of data, an excel sheet with proper validation rules was developed and implemented. EDCD has already launched and implemented DHIS 2 in central level in order to manage data that enables the creation of digital forms, indicators and reports, calculations of aggregate data including the displays of graphics including GIS.

The aim of this guideline is to assist medical recorders, physicians, public health workers and laboratory personnel, in diagnosing accurately communicable diseases subject to national and international surveillance, in timely reporting them, assist in the diagnosis by collecting proper laboratory sample, and undertaking control measures with an adequate understanding of the epidemiology of these diseases.

This guideline has been formulated based on deliberations held at the Epidemiology and Disease Control Division of Department of Health Service and the Vector Borne Disease Research & Training Centre, Hetauda. Information was also obtained by reviewing the literature available from WHO, CDC and other resources. A core group documented the guideline and a workshop finalized it.

I would like to thank all the contributors of this guideline.

June, 2016

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PART I: INTRODUCTION

Surveillance

Disease surveillance is the collection of information for action. By collecting information about cases of the disease and appropriately analyzing the data, one can determine what actions are needed to reduce the number of cases. Decision on resource allocation and on the definition of priorities and objectives, cannot be made without a database in order to identify problems and their pattern of distribution in the population. Surveillance data are used to:

- Evaluate the impact of programmes on the occurrence of diseases related to them in the community.
- Establish priorities among diseases.
- Identify specific population groups at high risk of illness and death, so that specific activities and resources can be used efficiently.
- Identify, investigate and control outbreaks or epidemics, as well as Emerging/ Re emerging diseases.

Surveillance does not have to be complex. In fact, a common problem with much surveillance system is that they are too complex. So much time is spent on collecting data that little time is left for taking actions that will reduce the number of cases of the disease. For this reason, it is important to collect only the data that is needed and will be used. Furthermore, action should be taken at the level at which the data are obtained. This is especially true for zonal /district hospitals, health centers and health posts, since it is at this level that most health services are provided. If District Health Officers, Public Health Officers and supervisors wait to take any action until feedback comes from the central level, it may be too late.

Surveillance: Information for action

Action may include:
Planning. A knowledge of disease incidence, morality and disability is required to obtain the resources needed to mount a disease control programme. It is also needed to plan programme strategies and to set realistic disease reduction targets. Available data are usually grossly inadequate for these purposes and often-special studies need to be carried out to illustrate the magnitude of the health problem.
Evaluation. Surveillance data are required to assess whether programme are having their expected impact in reducing disease incidence.

Outbreak investigation and control. As an example, increased immunization coverage reduces disease transmission. High coverage levels change the

epidemiological characteristics of disease such as measles, pertussis and poliomyelitis. The pattern of continuous endemicity is replaced by disease free intervals punctuated by outbreaks. Outbreak investigation is required to determine whether the cause is due to impotent vaccines (breaks on the cold chain), failure to immunize specific population or the gradual accumulation of susceptible resulting from a combination of less than 100% coverage and less than 100% vaccine efficacy. This principle can be adapted for any transmissible disease.

Methods of Surveillance

Method of disease surveillance includes routine reporting and sentinels sites reporting. In addition, there are other kinds of surveillance activities: case/ outbreak investigations and special studies (like surveys and activities). They all have their places in epidemiology.

Routine reporting

Routine reporting system – whether in development or developing countries – are notoriously incomplete, delayed and/or not accurate for most diseases; a study in the USA showed that only 35% of hospitalized cases of six infectious diseases were reported. Routine reporting becomes relatively complete only when the high priority of the diseases is recognized and when cases become less common.

In Nepal, health staffs collect information about the number of cases of reportable, communicable disease that occur in their catchments area. On a monthly basis, they send this information to the MIS, DHS.

As long as routine reports are reasonably consistent, they can be useful in evaluating disease trends; even though they underestimate actual diseases include and suffer from some deficiencies. Among these:

- Too many details are requested about cases of reportable diseases. This discourages recording and reporting at the service e level and complicates analysis of data at intermediate level of the health services.
- Not all cases come for treatment, and the reported number of cases depends largely on the extent to which the health facilities are frequently used, the reported number of cases may be higher than in other areas which actually have a many or more cases.
- Some diseases, such as Dengue, JE (Japanese Encephalitis) and Kala-azar, are more commonly treated at hospitals and therefore may be less likely to be reported at the health center or health/sub health post.
- Not all health facilities may report regularly, and some may have incomplete (or bad quality) reports. Thus, there may be missing or lost data. Even when reporting is fairly regular and complete, there may be

inconsistencies if health workers in the system follow different procedures and use different case definitions and guidelines (false positive reporting).

- Not all cases that are, in fact, seen and diagnosed by health institution staff are reported and investigated adequately (no action is taken at the site where the data are originally collected). Data analysis and subsequent action are regarded as function of the health ministry and not as a tool for self-evaluation by the staff at the local level, where reports originate.
- Health workers at the service level soon realize that it makes no difference what they report or even whether they report, if neither feedback nor orientation is received from the immediate superior levels.

Sentinel Reporting

Sentinel reporting uses data from a few selected sites rather than the data from all sites. It is particularly useful as a compliment to the routine system when routine reports are late, incomplete or inaccurate.

Sentinel surveillance is the collection and analysis of data by designated institutions selected for their geographic location, medical specialty, and ability to accurately diagnose and report high quality data. For example, district hospitals may be required to report specific conditions such as AGE in order to quantify the burden of disease. Generally, sentinel surveillance is useful for answering specific epidemiologic questions, but, because sentinel sites may not represent the general population or the general incidence of disease, they may have limited usefulness in analyzing national disease patterns and trends.

Sentinel reports can serve as a useful early warning system. Data from a sentinel hospital are available more quickly than the data from the districts as a whole and can provide an early warning of outbreaks. These health facilities report the number of cases of disease that occur for a specific time period. They will also be asked to report additional information, such as age, location, immunization status, etc., as well as weekly "ZERO" reports (no occurrence of cases).

Sentinel sites are chosen because they are likely to see cases of a certain disease in a certain age group, and their staff have been trained and motivated, and are willing to report timely, regularly and accurately.

Early Warning Reporting System (EWARS)

Early Warning Reporting System (EWARS) is a hospital-based sentinel surveillance system currently operational in 40 hospitals throughout Nepal. EWARS is designed to complement the country's Health Management Information System (HMIS) by providing timely reporting for the early

detection of selected vector-borne, water and food borne diseases with outbreak potential.
The hospital based reporting provides timely signal or alert and early detection of possible outbreak due to increased number of cases in the community leading to continuous transmission of the disease for timely response. This dynamics is lacking with HMIS being a monthly reporting system.

The main objective of EWARS is to strengthen the flow of information on vector borne and other outbreak prone infectious diseases from the districts; and to facilitate prompt outbreak response to be carried out by Rapid Response Teams (RRTs) at Central, Regional and District level, which can be mobilized at short notice to support the local levels (DHO/HP/SHP) in case investigation and outbreak control activities.
In the broader perspective, it also aids on program planning, evaluation, and the formulation of research hypotheses and to disseminate data/information on infectious diseases through appropriate feedback system

It was established in 1997 first in 8 sentinel sites and expanded to 24 sites in 1998, 26 sites in 2002, 28 sites in 2003 and 40 sites in 2008.

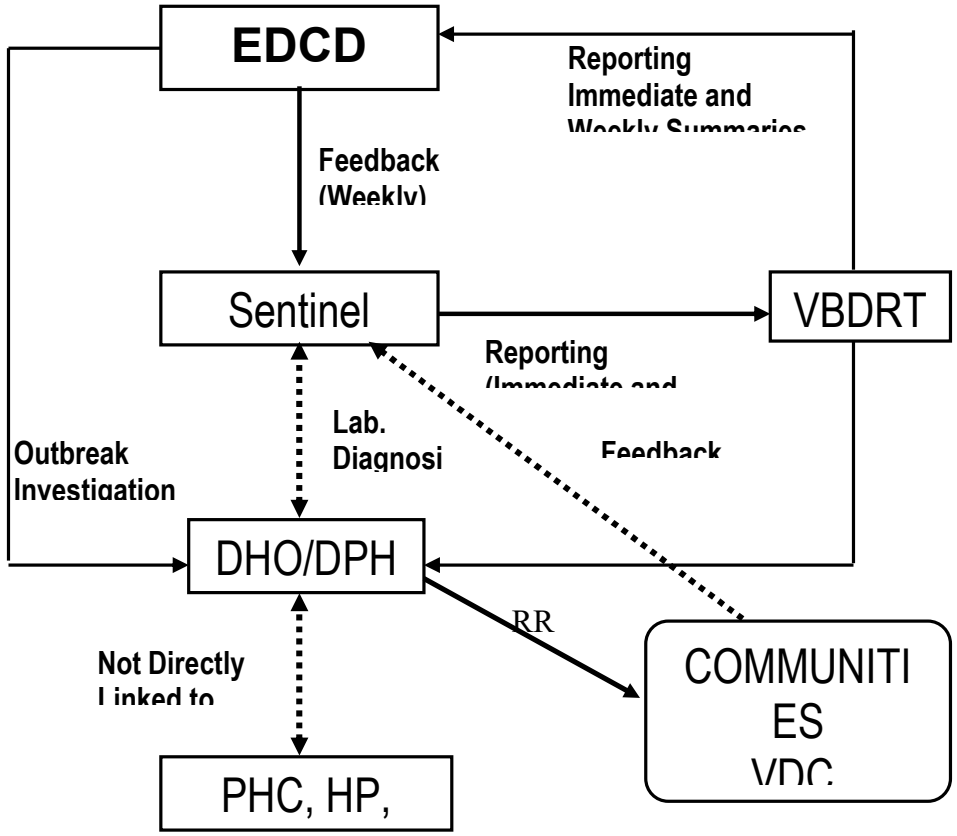
The EWARS mainly focuses on the **weekly reporting** of number of cases and deaths (including "zero" reports) of six priority diseases: three vector-borne diseases Malaria, Kala-azar and Dengue and three outbreak potential diseases Acute Gastroenteritis (AGE), Cholera and Severe Acute Respiratory Infection (SARI). It equally focuses on **immediate reporting** (to be reported within 24 hours of diagnosis) of one confirmed case of Cholera, and severe and complicated Malaria and one suspect/clinical case of Dengue as well as 5 or more than 5 cases of AGE and SARI from the same geographical locality in a one week period. Based on the experiences of reported outbreaks of acute diarrhoeal diseases and influenza by several districts, these two diseases are included for reporting in EWARS from the year 2005. Likewise, Dengue and DHF case reporting will be required to be reported in EWARS due to its high potential of impending epidemics. Other communicable diseases besides these six prioritized diseases also need to be reported in EWARS, whenever the numbers of cases exceed the expected level.

Information Flow Mechanism in EWARS:
(Sentinel site → VBDRTC →EDCD →feedback to districts/sites)

It is very important to understand this flow diagram describing the flow of information at different levels. Since, the response/actions are expected at each level. And it is equally important that the flow of information should be timely and regular, thus unduly delays are avoided for appropriate functioning of EWARS. The suspected cases of EWARS reportable diseases originate in the

community and attend the nearest health facilities and based on the capacity or availability of the services referred to district level hospitals. With respect to EWARS, the report (both immediate and weekly) is generated at the hospitals (district, zonal, regional and sub-regional, central and others) called the sentinel site. Each sentinel site sends those reports to VBDRTC, Hetauda and this institution consolidates the reports of all reporting sites and sends both immediate and weekly summaries to EDCD as well as to the respective public health offices- only the immediate reports requiring rapid actions. EDCD on receipt of the summaries prepares a weekly bulletin and disseminates to all sites and relevant stakeholders as a feedback for timely and appropriate actions.

Information Flow Diagram



EWARS is designed to complement the HMIS by providing systematic collection, collation, analysis, interpretation and dissemination of data on six identified diseases (mentioned above) for immediate

Reporting system: SENTINEL SITE LEVEL

Type and frequency:

a. **Type One- Immediate report (EWARS-2):** The sentinel hospitals prepare IMMEDIATE REPORT within 24 hours of confirmation of diagnosis (clinical and/or laboratory) of all EWARS reportable diseases except Kala-azar. The importance of reporting of those diseases are determined due to their high potentials to outbreaks, and targeted for disease control. In order to confirm to report immediately is guided by their threshold to report, likewise vector borne diseases (VBDs) one case of severe and complicated malaria, suspected Dengue/DHF; Airborne disease 5 cases of Severe Acute Respiratory Infection (SARI) in one week period from one locality and water/food borne diseases one case of confirm Cholera and 5 cases of Acute Gastroenteritis from one locality in one week period. The frequency will be every 24 hours.

b. **Type Two- WEEKLY Report (EWARS-3):** The sentinel hospitals prepare WEEKLY REPORT on the basis of epidemiological week calendar (starts on Sunday and ends on Saturday). Epidemiological week calendar for each calendar year starts on the first week of January, which will be Epidemiological Week 1 and ends on lasts week of December i.e. Epidemiological Week 52. For example for the year 2009 starts from December 28 (Epidemiological Week 1) and ends on December 26 (Epidemiological Week 52). The report of the week consists of the cases of this particular week including those reported in immediate reports. Thus, the frequency will be every week of the corresponding Epidemiological Week.

Collection, consolidation and transmission of reports

a. **Sentinel Site Level:**
Collection: The cases originating from the communities attend various departments of the hospitals depending on the nature of the cases like emergency, pediatric, medical and few/many may get admitted in the indoor department. Medical Recorder visits those departments everyday and fills up EWARS – 1 form (refer to the form and guideline below).

Recording Form

EWARS-1

Government of Nepal
Ministry of Health & Population
DoHS, EDCD, VBDRTC
EWARS Recording Form

Sentinel Site Name	
Email	
Year	

								Current Address					Disease			Lab Report			Outcome	
SN	Nepali Date [yyyy/mm/dd]	Registration No	OPD/Eme/IPD	Name of Patient	Age		Sex	District	VDC/Muni	WardNo	Village/Tole	Contact No	Disease Name	If Other, Specify	Diagnosis	Method	Result	Place of Test	Outcome	If Referred, Location/Institution
						Year														
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Prepared by:

Approved by:

Reporting Form

EWARS-2

WITHIN 24 HOURS

Government of Nepal
Ministry of Health & Population
DoHS, EDCD, VBDRTC
EWARS Recording Form

Sentinel Site Name	
Email	
Year	

							Current Address					Disease			Lab Report			Outcome	
SN	Nepali Date [yyyy/mm/dd]	Registration No	OPD/Eme/IPD	Name of Patient	Age	Sex	District	VDC/Muni	WardNo	Village/Tole	Contact No	Disease Name	If Other, Specify	Diagnosis	Method	Result	Place of Test	Outcome	If Referred, Location/Institution
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* If more than 5 cases from the same geographical area in a one-week period

Prepared by: Approved by:

Contact no. ☐ A copy provided to DHO/DPHO (RRT)

GUIDELINES FOR FILLING UP EWARS FORMS

EWARS - 1

Definition: Daily recording form for the six targeted diseases should be kept at the sentinel sites in register books/files. The compiled information (forms) can be utilized by the sentinel site/ DPHO/VBDRTC/EDCD to generate database for future actions.

Instructions for filling the form	
Sentinel Site Name	List of Sentinel site is provided, select your site.
Email	Contacts where this report is to be sent periodically (weekly)

Form Fields to be filled		
SN	Enter the serial number	
Nepali Date	Nepali date (BS) of the patient registration, please type Year-month-day (eg: 2015-10-16)	
Week No	The epidemiological week number which the patient is registered. List is provided, please select.	
Reg. No	Enter the hospital registration number of the patient.	
OPD/Eme/IPD	Please select type of patient registration (OPD/IPD/Emergency).	
Name of Patient	Enter full name of the patient	
Age	Age of the patient, please type whole number	
	Select Year or month or day for patient age.	
Sex	Select sex of the patient.	
District	**Address of the patient**	District, Select from the list.
VDC/Muni		VDC/Municipality, select from the list.
W.No		Ward number, select from the list.
Village/Tole		Type the name of village or tole
Contact No		Type the contact number of patient
Disease Name	**Disease which the patient was diagnosed**	Name of the disease, select from the list.
ICD Code		ICD code associated with the disease, automatically populated.
If Other, Specify		Type the disease name if others is selected in previous cell.
Diagnosis	Type of diagnosis, select among probable, confirmed and suspect.	
Method	**Lab report**	Method of the diagnosis, select from the list.

Result		Result of the lab test, select from the list.
Place		Place/Lab name where the test was performed.
Outcome	**Outcome**	Select the outcome.
If Referred, Location/Institution		If the outcome is 'referred', type the name of the health facility where the patient was referred.

Instructions for Report	
Week range	Select the range of weeks which you want to calculate the report. Week from is always smaller or equal to the week to.

Color Indicators	
Orange	In the form, the cell with this color indicates that some data is expected, when you type the required information the color disappears. If the outcome is 'Under Treatment', it indicates that this value should change later as per treatment result. In the report completeness indicator this color means that the data completeness is between 21% to 79% (Satisfactory).
Green	This color at the end of each row of the form indicates that data for the row is complete. In the completeness indicator, it indicates that the data completeness is equat or more than 80% (Excellent).
Red	This color at the end of each row of the form with 'Incomplete Data' label, indicates that the data for this row is incomplete, check if data entry is missing. In the report completeness indicator, this means that the completeness of the report is less than 20% (Poor).

EWARS - 2

Definition: This form is an immediate reporting (i.e., within 24 hours of attendance) form, which is faxed to VBDRTC (Fax Number : 057 - 520484) and carbon copied to EDCD and DPHO (RRT). It reports five diseases - Severe and Complicated Malaria, Dengue Fever/ Dengue Haemorrhagic Fever/ Dengue Shock Syndrome, Cholera (one case each) and AGE and SARI (more than 5 cases from a same locality in a week period). The reporting diseases and threshold of cases are as follows:

Severe & Complicated Malaria: 1 case = Immediate Report (within 24 hours after case confirmation) through EWARS-2 Form
Cholera = Immediate Report (within 24 hours after case confirmation) through EWARS-2 Form
DF/DHF/DSS: 1 case = Immediate Report (within 24 hours after case detection) through EWARS-2 Form.
AGE: The occurrence of 5 or more cases from the same locality or geographical area in a week period requires Immediate Report through EWARS-2 Form.
SARI: The occurrence of 5 or more cases from the same locality or geographical area in a week period requires Immediate Report through EWARS-2 Form.

Consolidation:

The records of cases of the week maintained in both EWARS Form-1 and EWARS Form –2 should compiled in EWARS Form –3.

Linkage with DPHO or Public Health Section in DHO

Transmission of reports:

A. Immediate reports: Consolidated immediate reports should be verified and signed by Medical Recorder and Medical Superintendent of the hospital and faxed to both EDCD (Fax number 01-4262268) and VBDRTC (Fax number 057-521826). The fax transmission result should be attached with the original report and filed for record (this helps in determining the timeliness and regularity)
B. Weekly reports: Consolidated weekly reports should be prepared for the epidemiological week and sent by fax to VBDRTC by Tuesday noon of the following week.

Timeliness: The timeliness and regularity of the report for that reporting week is categorized as follows:

a. **On time Report:** Report of following epidemiological week received at VBDRTC before Tuesday noon.
b. **Late Report**: Report of following epidemiological week received at VBDRTC before Friday noon.
c. **No Report**: Not receiving of Report till Friday noon at VBDRTC.

Completeness:

% Completeness: $\frac{\text{Total number of weeks with report}}{\text{Epidemiological Week No.}} \times 100 = \%$ of completeness.

Note:

If the reports cannot be sent through fax due to various reasons; it can be sent through courier and the duplicate of receipt should be kept for file record.

If either of the mechanism doesn't work, it is advisable and wise to inform/report VBDRTC and/or EDCD by telephone for timely action.

If you have access of internet send the report by e-mail for timely response, later send report by post.

Reporting system: VBDRTC, Hetauda

Vector-borne Disease Research and Training Center (VBDRTC) serves as a focal point for EWARS by receiving and consolidate all immediate and weekly reports sent from the sentinel hospitals.

VBDRTC has two functions:

a. Every immediate reports received from the sites are consolidated within the day the reports are received and sends to respective DHOs/DPHOs for action and also to EDCD
b. Weekly reports received from all sites within the reporting week are consolidated in 8 different tables as follows and sent to EDCD by e-mail and fax by Friday evening of the following week.

Function of EDCD in EWARS

EDCD compiles, analyzes and disseminated the weekly report as a feedback to the all sites by preparing a EWARS Bulletin.

The product of the week on National epidemiological information with importance of outbreaks for the week are disseminated to all sentinel sites including all major health institutions of 75 districts in Nepal. Along with the epidemiological report, recent developments in epidemiology in other countries, WHO fact sheets, WHO Press releases, CDC Atlanta fact sheets, epidemiological analysis of the outbreaks, public health related articles, reports and information on zoonotic diseases and Food safety and food borne illnesses are included on the back page of EWARS bulletin.

In addition to the above, EDCD facilitates in resource mobilization for EWARS related activities like printing of EWARS guidelines and forms, laboratory supplies, outbreak investigation with logistics and supplies, training and coordination with related organizations.

PART II: DISEASE DESCRIPTION

MALARIA

(ICD-10: B50-54)

IDENTIFICATION

Malaria is an infection that is due to parasite of the genus plasmodium in the blood or tissues infections with the four human malaria species can present sufficiently similar symptoms to make species differentiation generally impossible without laboratory studies. Furthermore, the fever pattern of the first few days of infection resembles that seen in early stages of many other illnesses (bacterial, viral and parasitic).

The most serious malarial infection, falciparum malaria (malignant tertian) may present a quite varied clinical picture, including fever, chills, sweats, cough, diarrhea, respiratory distress and headache, and may progress to icterus, coagulation defects, shock, renal and liver failure, acute encephalopathy, pulmonary and cerebral edema, coma and death. It is a possible cause of coma and other CNS symptoms, such as disorientation and delirium, in any non-immune person recently returned from a tropical area. Prompt treatment is essential,, even in mild cases, since irreversible complications may appear suddenly; case-fatality rates among untreated children and nonimmune adults can be 10%-40% or higher.

The other human malarias, vivax (benign tertian), malariae (quartan) and ovale generally are not life threatening. Illness may begin, with indefinite malaise and a slowly rising fever of several days' duration, followed by a shaking chill and rapidly rising temperature, usually accompanied by headache and nausea, and ending with profuse sweating. After an interval free of fever, the cycle of chills, fever and sweating is repeated, either daily, every other day or every third day. Duration of an untreated primary attack varies from a week to a month or longer. True relapses following periods with no parasitemia (seen with vivax and ovale iafections) may occur at irregular intervals for up to 5 years. Malariae infections may persist for life with or without recurrent febrile episodes.Persons who are partially immune or who have been taking prophylactic drugs may show an atypical clinical picture and a prolonged incubation period.

The most important method for diagnosis of malaria is the demonstration of malaria parasite in the peripheral blood film. For this purpose, blood smear (10-20 mm diameter) is taken onto a clean glass slide. When blood smear is dried, wrap the blood smear slide into a wrapping paper and sent to the laboratory as soon as possible for laboratory examination. If delay is anticipated for staining, fix the smear by adding 2-3 drop of pure methanol and dry at room temperature before

rapping by paper. Alternatively, blood sample can be collected onto what man No. 3 filter paper and dry at room temperature.
Repeated microscopic examinations every 12-24 hours may be necessary because the density of *Plasmodium falciparurn* parasites in the peripheral blood varies and parasites are often not demonstrable in films from patients recently or actively under treatment. The most promising are RDTs dipsticks that detect circulating plasmodial antigens in the bloodstream. Quality RDTs (Rapid diagnostic test) is a valuable component to microscopy because it helps expand the coverage of parasite load diagnosis to the periphery and minimize exclusively clinical diagnosis.

INFECTIOUS AGENTS

Plasmodium vivax, P. malariae, P. falciparum and *P. ovale,* sporozoan parasites. Mixed infections are not infrequent in endemic areas.

RESERVOIR

Humans are the only important reservoir of human malaria. Nonhuman primates are naturally infected by many malaria species, including *p. knowlesi, p. cynomolgi, P. brazilianum, P. inui, p. schwetzi* and *P. simium,* which can infect humans experimentally, but natural transmission to humans is rare.

MODE OF TRANSMISSION

By the bite of an infective female *Anophelses* mosquito. Most species feed at dusk and during early night hours; some important vectors have biting peaks around midnight or the early hours of the morning. When female *Anopheles* mosquito ingests blood containing the sexual stages of the parasite (gametocytes), male and female gametes unite to form the ookinete in the mosquito stomach which then penetrates the stomach wall to from a cyst on the outer surface in which thousands of sporozoites develop; this requires 8-35 days, depending on the species of parasite and the temperature to which the vector is expose. These sporozoites migrate to various organs of the infected mosquito, and some that reach the silvary glands mature and are infective when injected into a person as the insect takes the next blood meal.

In the susceptible host, the sporozoites enter liver hepatocytes and develop into exoerythrocytic schizonts. The hepatocytes rupture and asexual parasites (tissue merozoites) reach the bloodstream through the hepatic sinusoids and invade the erythrocytes to grow and multiply cyclically. Most will develop into asexual forms, from trophozoites to mature blood schizonts that rupture the erythrocyte within 48-72 hours, to release 8-30 (depending on the species) free erythrocytic merozoites that invade other erythrocytes. Clinical symptoms are produced at the time of each cycle, by the rupture of large numbers of erythrocytic schizonts. Within infected erythrocytes, some of the merozoites may develop into the male

(microgametocyte) or the female (macrogametocyte), the sexual forms.

The period between the infective bite and the detection of the parasite in a thick blood smear is the "prepatent period," which is generally 6 –12 days with *p. falciparum,* 8-12 days with *p. vivax* and *p. ovale,* and 12-16 days with *p. malariae* (but may be shorter or longer). Delayed primary attacks of some *p. vivax* strains may occur 6-12 months after exposure. Gametocytes usually appear in the blood stream within 3 days of parasitemia with *p. vivax* and *p. ovale,* and after 10-14 days with *p. falciparum.* Some exoerythrocytic forms of *p. vivax* and *p. ovale* exist as dormant froms (hypnozoites) that remain inhepatocytes to mature months or years later and produce relapses. This phenomenon does not occur in *faliciparum* or *malariae* malaria, and reappearance of these forms of the disease is the result of inadequate treatment or of infection with drugresistant strains. Malaria may also be transmitted by injection or transfusion of blood from infected persons or by use of contaminated needles and syringes, as by injecting drug users. Congenital transmission occurs rarely, but stillbirth from infected mothers is more frequent.

INCUBATION PERIOD

The time between the infective bite and the appearance of clinical symptoms is approximately 7-14 days for *P. faiciparum,* 8-14 days for *P. vivax and P. ovale,* and 7-30 days for *P. malariae,* With some strains of *P. vivax,* mostly from temperate areas, there may be a protracted incubation period of 8-10 months. With infection by blood transfusion, incubation periods depend on the number of parasites infused and are usually short, but may range up to about 2 months.

PERIOD OF COMMUNICABILITY

For infectivity of mosquitoes, as long as infective gametocytes are present in the blood of patients; this varies, with species and strain of parasite and with response to therapy. Untreated or insufficiently treated patients may be a source of mosquito infection for more than 3 years in *malariae*, 1-2 years in *vivax,* and generally not more than 1 year in *falciparum* malaria; the mosquito remains infective for life. Transmission by transfusion may occur as long as asexual forms remain in the circulating blood; with *p. malariae* this can continue for 40 years or longer. Stored blood can remain infective for at least a month.

SUSCEPTIBILITY AND RESISTANCE

Susceptibility is universal except in humans with specific genetic traits. Tolerance or refractoriness to clinical disease is present in adults in highly endemic communities where exposure to infective anophelines is continuous over many years. Persons with sickle cell trait have relatively low parasitemia when infected with *p. faiciparum,* and therefore are relatively protected from severe disease.

RATIONALE FOR SURVEILLANCE

Malaria continues to be one of the priority public health problems in Nepal, especially for those living in forested, forest fringe and foothills of southern Terai and inner Terai districts, where the risk of contracting the disease is far greater than the rest of the country. Malaria transmission is evident in 65 of the 75 districts in Nepal. An estimated 22.8 million (2007) people live in these districts and are at risk of malaria. The high risk is attributed to the abundance of vector - mosquitoes, mobile and vulnerable population, relative inaccessibility of the area, environmental and socio-economic factors. The epidemic potential is a real concern as evident from periodic outbreaks in the past including outbreak in Banke district in September/October 2006. Epidemics have occurred at regular intervals in 1985, 1991, 1996-97, 2002 and 2006.

RECOMMENDED CASE DEFINITION

Laboratory criteria for diagnosis:

- Demonstration of malaria parasite in the peripheral blood films
- Detection of malarial antigen by rapid diagnostic test kit, where microscope is not available.
- Detection of antibodies against malaria in the serum by indirect immunofluorescence (IFA) or enzyme linked immunosorbent assay (ELISA)
- Detection of malaria parasite by polymerase chain reaction (PCR)

Case classification

Probable severe malaria:
A person requiring hospitalization for symptoms and/or signs of severe malaria, who receives antimalarial treatment.

Confirmed Severe malaria:
A patient requiring hospitalization for symptoms and/or signs of severe malaria, with microscopy /RDT confirmation of diagnosis.

Confirmed uncomplicated malaria:
Confirmed uncomplicated malaria is defined as a symptomatic case of malaria without signs of
severity or evidence of vital organ dysfunction which is confirmed by microscopy or rapid diagnostic test.

Treatment failure:
A case of confirmed malaria with a history of having taken the correct dosage and followed the nationally recommended antimalarial treatment, but presents with asexual parasitemia on a blood smear within 14 days of the start of the treatment.

RECOMMENDED TYPES OF SURVEILLANCE FOR SENTINEL SITES

- Patient records should be maintained at Hospital level in each EWARS sentinel sites.
- Medical Recorders of EWARS sentinel sites should be maintained EWARS-1 register by recording of all confirmed malaria after consulting the Emergency register, Inpatient/OPD register, Laboratory register and other concerns registers.
- Medical Recorders of EWARS sentinel sites must report all cases of probable and/or confirmed severe & complicated malaria including within 24 hours on immediate reporting forms (EWARS-2).
- Medical Recorders of EWARS sentinel sites should reporting on all confirmed cases of Malaria in the weekly EWARS reporting form (EWARS-3) including zero reporting.
- Nursing In charge should be informed to Medical Recorder about all cases (probable/confirmed) of Severe Malaria admitted in any wards.
- Timely recognition of malaria epidemic and notification at all times; all **outbreaks** (clinical cases) should be reported **immediately** to the respective Regional Health service directorate and the EDCD/DHS and/ or VBDRTC/ Hetauda for immediate investigation and laboratory confirmation.

RECOMMENDED MINIMUM DATA

As per EWARS reporting forms and guidelines.

PRINCIPAL USES OF DATA FOR ACTION

- Identify high-risk groups and problem areas (e.g. districts where therapeutic efficacy of anti-malarial drugs studies must urgently be carried out) and micro stratification should be done by district in order to identify high-risk low risk and no risk areas/villages/ clusters.
- Evaluate impact of control measures
- Adjust and target control measures
- Guide allocation of resources and training efforts.
- Institutionalization of drug resistance monitoring.

SPECIFIC TREATMNT FOR ALL MALARIA

a) Management of severe malaria:

i) Clinical assessment

Severe malaria is caused by *P. falciparum* but not all *P.falciparum* malaria cases are severe. Severe malaria is a medical emergency. The airway should be secured in an unconscious patients and breathing and circulation assessed. An intravenous cannula should be inserted and immediate measurements of blood glucose (stick test), haematocrit /

haemoglobin, and parasitaemia and, in adults, renal function should be taken. Blood should be taken for cross-match, and (if possible) full blood count, platelet count, clotting studies, blood culture and full biochemistry should be conducted

The assessment of fluid balance is critical in severe malaria. Respiratory distress, in particular with acidotic breathing in severely anaemic children, often indicates hypovolaemia and requires prompt rehydration and, where indicated, blood transfusion. Symptoms in children may deteriorate suddenly. Mortality amongst pregnant women and children who develop severe malaria is particularly high.

ii) Diagnosis of severe malaria

The signs of severe malaria are nonspecific and they can occur in other febrile diseases such as meningitis, encephalitis, septicemia, typhoid fever, leptospirosis and viral infections that are common in malaria endemic area. Therefore, the clinical diagnosis of severe malaria must be confirmed by microscopic examination of thick and thin blood smear by an experienced laboratory technician, which is still the gold standard for the diagnosis of malaria.

iii) Specific treatment in severe malaria

Treatment should be started immediately after the diagnosis is suspected but blood must be taken immediately before starting treatment to confirm the diagnosis by microscopy if available and if not available or feasible then by RDTs.

- A drug regimen as recommended in the National Malaria Treatment Protocol should be used. It is essential that antimalarial treatment in full doses is given as soon as possible in severe malaria.
- The antimalarial drug should be given parenterally preferably iv.
- Drugs should be given orally as soon as patient is able to take oral medication.

I. Dose of artesunate: Severe malaria is a medical emergency. Parenteral (IV) artesunate is the drug of choice for severe malaria (table 1). After rapid clinical assessment of the patient, a full dose of parenteral antimalarial treatment should be started without delay with whichever effective antimalarial is first available.

Table 1: Dose of artesunate in severe malaria

Groups	Drug	Dose	Remarks
Children: >1 year of age or > 5 kg. body weight	Artesunate I.V. or Artemether I.M.	2.4 mg/kg bw* i.v. on admission (time = 0h), then at 12 h and 24 h, then once a day. 3.2 mg/kg bw i.m. on admission then 1.6 mg/kg bw per day	Patient able to take oral medication then switch to oral ACT(6 doses over 3 days)
Adults	Artesunate I.V.	2.4 mg/kg bw i.v. on admission (time = 0h), then at 12 h and 24 h, then once a day	Patient able to take oral medication then switch to oral ACT(6 doses over 3 days)
Pregnancy in 2nd. and 3rd. trimester	Artesunate I.V.	2.4 mg/kg bw i.v. on admission (time = 0h), then at 12 h and 24 h, then once a day	Patient able to take oral medication then switch to oral ACT(6 doses over 3 days)

bw* = body weight

Artesunate is soluble in water but has poor stability in aqueous solutions at neutral or acid pH. In the injectable form, artesunic acid is drawn up in sodium bicarbonate to form sodium artesunate immediately before injection.

Oral Medication:
Once patient is available to take oral medication, treatment is switched to oral ACT and complete course is given.

II. Treatment with Quinine for Children less than 1 year and pregnant women in 1st. trimester of pregnancy.

Loading dose:
Quinine dihydrochloride 20 mg. salt per kg. body weight diluted in 5% dextrose or dextrose saline (10ml/kg body weight) given by intravenous infusion over a period of four hours.

Maintenance dose:
Quinine dihydrochloride 10 mg salt/kg body weight diluted in 5% dextrose or dextrose saline (10ml/kg body weight) given by intravenous infusion.

In adults, the maintenance dose is infused over a period of **four hours** and the dose is repeated every eight hours until the patient is able to take oral medication.
In children, the maintenance dose is infused over the period of **two hours** and repeated every 12 hours until the patient is able to take oral medication.

Oral dose:
When the patient is able to take oral medication then oral quinine sulphate tablets (10 mg. salt/kg. body weight) is given every eight hour to complete a seven day course of the quinine treatment.
Please note that:

- Intravenous quinine should be administered at recommended dosage for the first 48 hours even if acute renal failure or severe jaundice is present, but subsequent dosage should be reduced to half if IV infusion is necessary.
- Quinine infusion is **drug of choice in the first trimester of pregnancy and children < 1 year of age or < than 5 kg. body weight.**
- Continuous and uniform inflow of intravenous quinine is to be ensured, as a slow infusion will not achieve therapeutic concentration while too rapid infusion may induce cardiac toxicity.
- Monitor pulse, BP at least every 6 hours while the patient is on quinine therapy.
- Avoid erect posture of the acutely sick patient during quinine therapy to prevent postural hypotension.
- If the volume of overload is suspected, the volume of the infusion fluid for the administration of quinine can be reduced to half (i.e., quinine dihydrochloride 10 mg. salt/ 5 ml./kg. body weight). However, the duration of infusion is the same as above.
- If the IV infusion is not possible, quinine dihydrochloride can be given by intramuscular injection in the same dosage. The quinine should be diluted in normal saline to a concentration of 60-100mg salt/ml. The diluted quinine is divided into two equal parts and administered in two anterior thighs (one part in each thigh), not in buttock).

Intramuscular injections
Quinine dihydrochloride are acidic (pH 2) and cause pain, focal necrosis and in some cases abscess formation, and in endemic areas are a common cause of sciatic nerve palsy. Hypotension and cardiac arrest may result from rapid intravenous injection. Intravenous quinine should be given only by infusion, never injection.
If there is no improvement of clinical conditions after 48 hours of parenteral therapy, the maintenance dose of the parenteral quinine should be reduced by one third to one half (i.e., 5 – 7 mg. quinine dihydrochloride).

III. Other Drugs:

The use of following drugs in the management of severe malaria is of no beneficial effect and may indeed be harmful and should be avoided:

- Corticosteroids
- Other anti-inflammatory agents
- Agents given for cerebral oedema such as urea, mannitol.
- Low molecular weight dextran
- Epinephrine
- Heparin.

b. Treatment of uncomplicated confirmed malaria

Microscopy is the basis of diagnosis of malaria in hospitals. The use of RDTs in these facilities is justified only during off hours when microscopy is not feasible.

i) Treatment of vivax malaria

Chloroquine is the drug of choice in the treatment of *P. vivax* malaria. In addition, Primaquine is added for radical cure as *P.vivax* tends to relapse frequently. Primaquine is effective for the prevention of relapses. Therefore, chloroquine and primaquine should be administered to the patient according to the dosages given in table 2.

Table 2. Dosage of Chloroquine and primaquine by age group

Days	Drug	Age in years				
		< 1	1 - 4	5 – 9	10 – 14	> 14
1	Chloroquine tablet (150mg.)	½	1	2	3	4
	Primaquine tablet (7.5 mg.)	Nil	½	1	1 ½	2
2	Chloroquine tablet (150 mg.)	½	1	2	3	4
	Primaquine tablet (7.5 mg.)	Nil	½	1	1 ½	2
3	Chloroquine tablet (150 mg.)	½	½	1	1 ½	2
	Primaquine tablet (7.5 mg)	Nil	½	1	1 ½	2
4 – 14*	Primaquine tablet (7.5 mg.)	Nil	½	1	1 ½	2

Note : * = Standard 14 days Primaquine treatment is recommended if adequate monitoring and follow up can be ensured.

ii) Treatment of falciparum malaria

1. Oral Artemether and Lumefantrine (AL as CoartemR) fixed dose combination) in 6 doses over 3 days is the recommended first line

treatment of uncomplicated confirmed falciparum malaria (as detailed in table 3 below).

Table 3. The dosages of AL (CoartemR) by kg body weight

Body weight (kg.)	Day-1		Day-2	Day-3
	First dose (0 hour)	12 hours later	Twice daily -12 hours apart	
5-14	1 tablet	1 tablet	1 tablet	1 tablet
15-24	2 tablets	2 tablets	2 tablets	2 tablets
25-34	3 tablets	3 tablets	3 tablets	3 tablets
35 and above	4 tablets	4 tablets	4 tablets	4 tablets

- *AL should be given with meals preferably fatty meals (biscuits/milk)*
- *Persons with known hypersensitivity to the drug components should* not be treated with AL.
- *It is not given to children less than 1 year of age or patients with less than 5 kg body wt. It is not given during the first trimester of pregnancy.*
- *Oral quinine is the recommended second line drug for such cases.*

Table 4. Dosage of Quinine sulphate by body weight in Kg or age

Weight (Kg)	Age (years)	mg/ (Number of tablet(s)) 3 times a day
5 –10	2-11 months	75 mg. (1/4)
10.1-14	1-2	150 mg (1/2)
14.1-20	3-5	225 mg (3/4)
20.1-30	6-8	300 mg (1)
30.1-40	9-11	375 mg (1+1/4)
40.1-50	12-13	450 mg (1+1/2)
>50	14+	600 mg (2)

Quinine sulphate is available as 300 mg tablets

KALA-AZAR

(ICD-10: B55.0)

IDENTIFICATION

A chronic systemic disease caused by intracellular protozoa of the genus *leishmania.* The disease is characterized by fever, hepatosplenomegaly, lymphadenopathy, anemia, leucopenia, thrombocytopenia and progressive emaciation and weakness. Untreated clinically evident disease is usually fatal. Fever is of gradual or sudden onset, persistent and irregular, often with two daily peaks, with alternating periods of apyrexia and low-grade fever. Post-kala-azar dermal lesion may occur after apparent cure of systemic disease.

The rapid dipstick "rK39"test is the mainstay in the serological diagnosis of kala-azar. Demonstration of Leishmania Donovani is the most specific test for the diagnosis of kala-azar. This can be done by examination of bone marrow or splenic aspirate. Examination of aspirates from these sites is recommended since the concentration of the parasites is high at these sites. Since the specificity and the sensitivity of these tests are very high, these tests are considered as the "gold standard" for the diagnosis of kala-azar. However, the procedures are invasive with risks to the patient, and therefore not recommended for routine use in the programme. Only trained personnel should carry out these tests in well-equipped hospitals, to minimize the risk of complications.

INFECTIOUS AGENTS

Leishmania donovani

RESERVOIR

Humans are the only known reservoir in India, Nepal and Bangladesh.

Mode of transmission

Through bite of infected *phlebotomine* sand flies

INCUBATION PERIOD

Generally 2-6 months; range is 10 days to years.

PERIOD OF COMMUNICABILITY

Not usually transmitted from person to person, but infections to sand flies as long as parasites in the circulating blood or skin of the mammalian reservoir host. Infectivity for *phlebotomines* may persist even after clinical recovery of human patients.

SUSCEPTIBILITY AND RESISTANCE

Susceptibility is general. Kala-azar apparently includes lasting homologous immunity. Considerable evidence indicates that inapparent and subclinical infections are common and that malnutrition predisposes to clinical disease and activation of inapparent infections. Manifest disease occurs among AIDS patients, presumably as reactivation of latent infections.

RATIONALE FOR SURVEILLANCE

Kala-azar is endemic in 12 districts of central and eastern regions of Nepal. Nearly six million people residing in these districts which bordering with Bihar state of India. At risk of acquiring this disease sporadic cases are also recorded in the western part of country. Kala-azar is a re-emerging disease of chronic nature. If untreated the disease can be fatal. Thus for the sake of timely detection and proper and adequate treatment of kala-azar cases is essential.

RECOMMENDED CASE DEFINITION

Patients with kala-azar have fever (of more than two weeks), splenomegaly, anaemia and weight loss. A person from an endemic area with fever of more than two weeks and has splenomegaly should be tested for kala-azar.

Laboratory criteria for diagnosis –

- Demonstration of LD bodies in the smear prepared from bone marrow, spleen and peripheral blood samples
- Detection of parasite specific antigen by rapid diagnostic test kit eg. rK-39 test
- Detection of parasite by immunofluorescence assay (IFA) or enzyme linked immunosorbent assay (ELISA)
- Detection of parasite DNA by polymerase chain reaction (PCR)

Case classifications

- **Probable:** a person visiting from or residing in Kala–azar endemic area and having fever of more than two weeks with or without splenomegaly, malaria parasites negative during repeated blood slide examination and not responding to standard treatment with anti malarial drugs.
- **Confirmed :** A VL case is a person showing clinical signs (mainly prolonged irregular fever of more than two weeks, hepato-splenomegaly, anaemia and weight loss) with parasitological confirmation (LD bodies positive in stained smears from bone marrow, spleen, liver, lymph node, blood or by culture) or rK – 39 positive.

RECOMMENDED TYPES OF SURVEILLANCE FOR SENTINEL SITES

- Patient records should be maintained at Hospital level in each EWARS sentinel sites.
- Medical Recorders of EWARS sentinel sites should be maintained EWARS-1 forms by recording of all clinical case/s

(probable/confirmed) of Kala-azar after consulting the case investigation forms, Emergency register, Inpatient/OPD register, Laboratory register and other concerns registers.

- Medical Recorders of EWARS sentinel sites should reporting on all clinical case/s (probable/confirmed) of Kala-azar in the weekly EWARS reporting form (EWARS-3) including zero reporting.
- Nursing In charge should be informed to Medical Recorder about all clinical case/s (probable/confirmed) of Kala-azar admitted in any wards.

RECOMMENDED MINIMUM DATA

As per EWARS reporting forms and guidelines.

PRINCIPAL USES OF DATA FOR ACTION

- Evaluate the real extent of the problem and the main populations at risk
- Improve and focus the control activities
- Identify technical and operational difficulties
- Evaluate impact of control interventions
- Anticipate epidemics, apply epidemic preparedness, epidemic containment

SPECIFIC TREATMENT

1. **First- line drug- Miltefosine:** Miltefosine is a relatively safe oral drug for the treatment of kala-azar.

Recommended dose schedule

Adults (>25 Kg body weight) 50 mg capsule morning and 50 mg evening after food

Adults <25 kg body weight 50 mg in the morning after food

Children (2-11 years age) 2.5 mg/kg daily in two divided doses after food

Duration of treatment

Miltefosine should be given daily at the dose mentioned above for a period of 28 days. In cases of missed doses treatment up to 35 days is recommended to complete the full course.

When to avoid the use of miltefosine

Miltefosine is the preferred first-line drug in all patients of kala-azar except the following:

- Women during pregnancy
- Married women of child-bearing age who are not using contraceptives regularly and are “at risk” of becoming pregnant
- Women who are breast-feeding their babies
- Infants

Miltefosine may not be the ideal drug for patients of kala-azar with severe under nutrition, severe anaemia and patients with known history of kidney or liver

disease

For patients with severe anaemia and severe undernutrition, before starting miltefosine treatment should be built up by blood transfusion to correct anaemia and appropriate feeding to correct severe undernutrition. If dehydration is present, it should be corrected with fluids, preferably oral reydration solution (ORS). This would help in reducing the side effects of the drug.

Side effects and their treatment

Miltefosine may cause mild vomiting and diarrhoea during the first week of treatment in some patients. The patient should be advised to take sips of ORS solution (or any other liquid if ORS is not available) frequently. If the vomiting is severe the patient should be restarted with ORS very slowly. If vomiting does not stop, despite the use of ORS, the patient should be administrating IV fluid. Diarrhoea is usually self-limited and should be treated with ORS. Severe cases of diarrhoea require IV-fluid administration (Ringer's lactate). Additional antibiotics are generally not recommended. There may be liver-or kidney-related side effects like puffiness of the eyes, jaundice or decreased urine.

2. Second-line drugs

The second line drugs are recommended in the following cases:

- Patient not responding to the first-line of drug or the drug was discontinued due to toxic effect.
- Women during pregnancy
- Women who are breast-feeding their babies
- Children less than two years of age.
- Kala-azar patient with liver or kidney disease.

i) Amphotericin B is the recommended second-line drug. Ambisome (Liposomal Amphotericin B) is also recommended as a second line of drug, but the drug is costly. The side effects should be diagnosed and treated promptly to prevent complications and death. The second-line drugs have to be given parenterally (IV route). The patient who is given second-line drugs should therefore be admitted to the hospital.

Amphotericin B deoxycholate 1 mg/kg daily is recommended in the form of daily IV infusion (in 5% dextrose solution) for 15 to 20 days, for achieving a cure rate of >90%.

Side effects of Amphotericin B include fever with chills and rigors. Generally they can be controlled by paracetamol and anti-histaminics. Rarely hydrocortisone may be required.

Hypokalaemia, nephropathy and myocarditis are occasionally associated with Amphotericin B administration.

The infusion should be given slowly over a period of six hours.

ii) Liposomal amphotericin B

Liposomal amphotericin B is given intravenously in a dose of 3mg/kg for five days or 5 mg/kg for three days is safe, has no side effects and shows a cure

rate >95%.

Studies have also shown that a single dose 5 mg/kg given IV has a cure rate >90%. However, large scale trials on single-dose treatment are not yet available.

Public sector undertakings can purchase this drug for distribution through public sector at preferential price. This can mean considerable cost cutting for the programmes

3. Newer first line drugs – Paramomycin

Paramomycin is a promising new effective drug. Paramomycin has been registered for use in India. Phase III trials underway in India. Phase IV trials planned in Nepal. Drug being registered in Nepal.

- The recommended dose is 15 mg/kg/day to be given by intramuscular (IM) injections for 21 days.
- The medicine is safe with minimal ototoxicity or nephrotoxicity. In the recommended dose, the ototoxicity is reversible.
- Paromomycin should be avoided in patients with severe anaemia with hemoglobin <5 g/dl.
- Pain in injection site is common.

DENGUE FEVER
(ICD-10: A 90)
DENGUE HAEMORRHAGIC FEVER (DHF)
DENGUE SHOCK SYNDROME (DSS)
(ICD-10: A 91)

IDENTIFICATION

Dengue Fever is an acute febrile viral disease characterized by sudden onset, fever for 3-5 days (rarely more than 7 and often biphasic), intense headache, myalgia, arthralgia, retro-orbital pain, anorexia, GI disturbances and rash. Early generalized erythema occurs in some cases. A generalized maculopapular rash usually appears about the time of defervescence. Minor bleeding phenomena, such as petechiae, epistaxis or gum bleeding may occur at any time during the febrile phase. Dark skinned races frequently have no visible rash. With underlying conditions, adults may have major bleeding phenomena, such as GI hemorrhage in peptic ulcer cases or menorrhagia. Recovery may be associated with prolonged fatigue and depression. Lymphadenopathy and leukopenia with relative lymphocytosis are usual; thrombocytopenia (less than 100 X 103/ cu. mm; SI units less than 100 X 109/L) and elevated transaminases occur less frequently. Epidemics are explosive, but fatalities in the absence of dengue hemorrhagic fever are rare.

Differential diagnosis includes all epidemiologically relevant diseases listed under arthropod-borne viral fevers, yellow fever, measles, rubella, malaria, leptospirosis and other systemic febrile illnesses, especially those accompanied by rash. HI, CF, IgG and IgM ELISA, and neutralization tests are diagnostic aids. IgM antibody, indicating current or recent infection, is usually detectable by day 6–7 after onset of illness. Virus is isolated from blood by inoculation of mosquitoes, or into mosquito or vertebrate cell cultures, and then identified with serotype specific monoclonal antibodies.

Dengue Haemorrhagic Fever (DHF) / Dengue Shock Syndrome (DSS) is a severe mosquito transmitted viral illness endemic in much of South and Southeast Asia, the Pacific and Latin America; it is characterized by increased vascular permeability, hypovolemia and abnormal blood clotting mechanisms. It is recognized principally in children, but occurs also in adults.

Illness is biphasic; it begins abruptly with fever and, in children, with mild upper respiratory complaints, often anorexia, facial flush and mild GI disturbances. Coincident with defervescence and decreasing platelet count, the patient's condition suddenly worsens, with marked weakness, severe restlessness, facial pallor and often diaphoresis, severe abdominal pain and circumoral cyanosis. The liver may be enlarged, usually 2 or more days after defervescence.

Hemorrhagic phenomena are seen frequently and include scattered petechiae, a positive tourniquet test, easy bruisability, and less frequently, epistaxis, bleeding at venipuncture sites and gum bleeding. GI hemorrhage is an ominous prognostic sign that usually follows a prolonged period of shock. In severe cases, findings include accumulation of fluids in serosal cavities, low serum albumin, elevated transaminases, a prolonged prothrombin time and low levels of C3 complement protein. DHF cases manifesting severe liver damage with or without encephalopathy have been observed during large epidemics of dengue-3 in Indonesia and Thailand. Case-fatality rates in untreated or mistreated shock have been as high as 40%-50%; with good physiologic fluid replacement therapy, rates should be between 1%-2%.

Serological tests show a rise in antibody titre against dengue viruses. IgM antibody, indicating a current or recent flavivirus infection, is usually detectable by day 6-7 after onset of illness. Virus can be isolated from blood during the acute febrile stage of illness by inoculation of mosquitoes or cell cultures. Isolation from organs at autopsy is difficult, but chances are improved by mosquito inoculation. Virus specific nucleic acid sequences may be detected by PCR.

INFECTIOUS AGENT

The viruses of dengue fever are *flaviviruses* and include serotypes 1, 2, 3 and 4 (dengue–1, 2, 3, 4). The same viruses are responsible for dengue hemorrhagic fever.

RESERVOIR

The viruses are maintained in a human *Aedes aegypti* mosquito cycle in tropical urban centres; a monkey mosquito cycle serves as a reservoir in Southeast Asia and West Africa.

MODE OF TRANSMISSION

By the bite of infective mosquitoes, principally *Ae. aegypti.* This is a day biting species, with increased biting activity for 2 hours after sunrise and several hours before sunset. Both *Ae. aegypti* and *Ae. albopictus* are found in urban settings; *Ae. albopictus,* which is abundant in much of Asia, is less anthropophilic than *Ae. aegypti* and hence is a less efficient epidemic vector. In Polynesia, one of the *Ae. scutellaris* spp. complex serves as the vector. In Malaysia, *Ae. niveus* complex and in West Africa *Ae. furcifer-taylori* complex mosquitoes are involved in enzootic monkey mosquito transmission.

INCUBATING PERIOD

From 3 to 14 days, commonly 4-7 days.

PERIOD OF COMMUNICABILITY

Not directly transmitted from person-to-person. Patients are infective for mosquitoes from shortly before to the end of the febrile period, usually a period of 3-5 days. The mosquito becomes infective 8-12 days after the viremic blood meal and remains so for life.

SUSCEPTIBILITY AND RESISTANCE

Susceptibility in humans is apparently universal, but children usually have a milder disease than adults. Recovery from infection with one serotype provides lifelong homologous immunity but does not provide protection against other serotypes and may exacerbate subsequent infections.

In DHF/DSS the risk factor described best is the circulation of heterologous dengue antibody, acquired passively in infants or actively from an earlier infection. Such antibodies may enhance infection of mononuclear phagocytes through the formation of infectious immune complexes. Geographic origin of dengue strain, age, gender and human genetic susceptibility are also important risk factors.

RATIONALE FOR SURVEILLANCE

Dengue fever, including DHF and DSS, is the most significant arthropodborne viral disease worldwide. It occurs in over 100 countries and territories and threatens the health of over 2500 million people in tropical and subtropical regions. Dengue fever is a severe disease with high epidemic potential.

RECOMMENDED CASE DEFINITION

DENGUE FEVER

Clinical description

An acute febrile illness of 2-7 days duration with 2 or more of the following:
Headache, retro-orbital pain, myalgia, arthralgia, rash: initially macular and blanching, later on mobilliform, haemorrhagic manifestations, leucopenia (WBC< 5000 cells /cumm.)

Laboratory criteria for diagnosis

One or more of the following:

- Isolation of the dengue virus from serum, plasma, leukocytes, or autopsy samples
- Demonstration of a fourfold or greater change in reciprocal IgG or IgM antibody titres to one or more dengue virus antigens in paired serum samples
- Demonstration of dengue virus antigen in autopsy tissue by immunohistochemistry or immunofluorescence or in serum samples by EIA
- Detection of viral genomic sequences in autopsy tissue, serum or CSF samples by polymerase chain reaction (PCR)

Case classification

Suspected: A case compatible with the clinical description.

Probable: A case compatible with the clinical description with **one or more** of the following:

- Supportive serology (reciprocal haemagglutination-inhibition antibody titre $\geq$ 1280
- Comparable IgG EIA titre or positive IgM antibody titre in late acute or convalescent-phase serum specimens.
- Occurrence at same location and time as other confirmed cases of dengue fever.

Confirmed: A case compatible with the clinical description and laboratory confirmed.

DENGUE HAEMORRHAGIC FEVER

A probable or confirmed case of dengue **and**

Haemorragic tendencies evidenced by **one or more** of the following:

- Positive tourniquet test
- Petechiae, ecchymoses or purpura
- Bleeding: mucosa, gastrointestinal tract, injection sites or other
- Haematemesis or melaena

And thrombocytopenia (100 000 cells or less per mm^3)

And evidence of plasma leakage due to increased vascular permeability, manifested by one or more of the following:

- $\geq$ 20% rise in average haematocrit for age and sex
- $\geq$20% drop in haematocrit following volume replacement treatment compared to baseline
- signs of plasma leakage (pleural effusion, ascites, hypoproteinaemia)

DENGUE SHOCK SYNDRCME

All the above criteria, **plus** evidence of circulatory failure manifested by rapid and weak pulse, and narrow pulse pressure ($\leq$20 mm Hg) or hypotension for age, cold, clammy skin and altered mental status.

RECOMMENDED TYPES OF SURVEILLANCE FOR SENTINEL SITES

- Patient records should be maintained at Hospital level in each EWARS sentinel sites.
- Medical Recorders of EWARS sentinel sites should be maintained EWARS-1 register by recording of all clinical case/s (suspected/probable/confirmed) of Dengue Fever including DHF & DSS after consulting the case investigation forms, Emergency register, Inpatient/OPD register and other concerns registers.
- Medical Recorders of EWARS sentinel sites must report of each clinical case (suspected/probable/confirmed) of Dengue Fever including DHF & DSS within 24 hours on immediate reporting forms (EWARS-2).
- Medical Recorders of EWARS sentinel sites should reporting on all clinical case/s (suspected/probable/confirmed) of Dengue Fever including

DHF & DSS in the weekly EWARS reporting form (EWARS-3) including zero reporting.

- Nursing In charge should be informed to Medical Recorder about all clinical case/s (suspected/probable/confirmed) of Dengue Fever including DHF & DSS admitted in any wards.
- All clinical case/s (suspected/probable/confirmed) of Dengue Fever including DHF & DSS should be reported immediately to the respective DHO/DPHO, Regional Health Services Directorate, and the EDCD/DHS for immediate investigation and, if possible, laboratory confirmation.

RECOMMENDED MINIMUM DATA ELEMENTS

As per EWARS reporting forms and guidelines.

PRINCIPAL USES OF DATA FOR DECISION-MAKING

- Evaluate the real magnitude of problems
- Target high risk areas for intervention – i.e. risk approach for interventives
- Monitor changes in serotype and rate of DHF / DSS.
- Monitor trends in endemic disease or re-emergence of disease

SPECIFIC TREATMENT

1. **Febrile phase:** Rest, Paracetamol (not more than 4 times in 24 hrs_according to age for fever above 39^0C.

Aspirin can cause gastritis and /or bleeding .In children, Reye's syndrome (Encephalopathy) may be a serious complication.

Age	Dose (syrup 125 mg/5ml)	mml/dose/d
<1 year	1/2 teaspoonful	2.5ml
1-4 years	1 teaspoonful	5ml
5 years and above	2 teaspoonful	10ml

- Do not give antibiotics as these do not help
- Oral Rehydration Therapy is recommended for patients with moderate dehydration caused by vomiting and high temperature.
- Food should be give according to appetite.

2. **Afebrile phase**

A. Dengue Fever

Constitutional symptoms in patients with DF after the fall of fever are as during the febrile stage. Most patients will recover without complication. Treatment should be carried out as indicated in chart 1.

i. Criteria for admission : Any of the following in the presence of suspicion of dengue fever :
   - Restlessness or lethargy
   - Cold extremities

   or circulatory failure

- Bleeding in any form
- Oliguria or Relucttance to drink fluids
- Rapid and Weak pulse
- Capillary refill time >2 seconds
- Narrowing of pulse pressure(<20mmhg)or hypotension
- Haematocrit of 40,or rising Haematocrit
- Platelet count of less than 100,000/mm3
- Acute abdominal pain
- Evidence of Plasma Leakage, e.g.pleural effusion, ascites

Patients refuses for admission,Should be adviced to:

- Encourage to drink fluids eg.ORS,fruit
- observe for coldness /blueness of extremities
- Asminister paracetamol for fever 10-15/kg/dose 4-6 hourly (limit to 5 doses in 24 hours)
- Tepid sponging as necessary
- Avoid aspirin and non steroidal anti-inflammatory drugs like brufen

The patient is brought back immediately to the nearest hospital in the presence of any one of the following situations:

- Not drinking/feeding
- Passing less urine than usual
- Abdominal pain or bleeding in any form
- In older children, inability to sit up,giddiness
- Irritability,drowsiness,restlessness
- Patient continues to unwell

B. For DHF/DSS: As in DF, during the afebrile phase of DHF Grades I and II, the patient has the same symptoms as during the febrile phase. The clinical signs plus thrombocytopenia and haemoconcentration or rise haematocrit are sufficient to establish a clinical diagnosis of DHF. During the phase, the patients should be observed for at least 2-3 days after the fall in temperature, for rashes on the skin, bleeding from nose or gum, blue spots on the skin or tarry stools. If any of these signs are observed, the patients should be brought to the hospital without delay. The only difference between the DF and DHF grade 1 is the presence of thrombocytopenia and rise in haematocrit (>20%)

Chart 1: DF/DHF Management charts

Febrile phase	**Manifestations**	**Management**
Duration 2-7 days	-Temp 30-40Oc -Headache -Retro-orbital pain -Muscle pain -Joint/bone pain -Flushed face -Rash -Skin haemorrhage, bleeding from nose,gums -Positive tourniquet test -Liver often enlarged -Leucopenia -Platelet/haematocrit normal	-At home -Bed rest -Keep the body Temperature below 39o -Paracetamol -yes -Aspirin -No -Brufen -No -Oral fluid and electrolyte therapy -Follow-up for any change in platelet/haematocrit

Afebrile phase (critical stage)	**Manifestations**	**Management**
Duration - 2-3 days after febrile stage	- same as during febrile phase - Improvement in general condition - Platelet/haemotocrit normal -Appetite rapidly regained	-Bed rest - Check platelet haematocrit - Oral fluids and electrolyte therapy

Convalescence phase	Manifestations	Management
Duration - 7-10 days after critical stage	- Further improvement in general condition and return of appetite - Bradycardia -Confluent petechial rash with white centre/ itching - Weakness for 1 or 2 weeks	- No special advice - No restrictions - Normal diet

ACUTE GASTROENTERITIS

Viral gastroenteritis presents as an endemic or epidemic illness in infants, children and adults. Several viruses (rotaviruses, enteric adenoviruses, astroviruses and caliciviruses including Norwalk-like viruses) infect children in their first years of life and cause a diarrheal illness that may be severe enough to produce dehydration requiring hospitalization for rehydration. Viral agents such as Norwalk-like viruses are also common causes of epidemics of gastroenteritis among children and adults. The epidemiology, natural history and clinical expression of enteric viral infections are best understood for type A rotavirus in infants and Norwalk agent in adults.

IDENTIFICATION

I. ROTAVIRAL ENTERITIS (ICD-10: A08.0)
(Sporadic viral gastroenteritis, Severe viral gastroenteritis of infants and children)

A sporadic, seasonal, often severe gastroenteritis of infants and young children is characterized by vomiting, fever and watery diarrhea. Rotaviral enteritis is occasionally associated with severe dehydration and death in young children. Secondary symptomatic cases among adult family contacts can occur, although subclinical infections are more common. Rotavirus infection has occasionally been found in pediatric patients with a variety of clinical manifestation, but the virus is probably coincidental rather than causative in these conditions. Rotavirus is a major cause of nosocomial diarrhea of newborns and infants. Although rotavirus diarrhea is generally more severe than acute diarrhea due to other agents, illness caused by rotavirus is not distinguishable from that caused by other enteric viruses for any individual patient.

Rotavirus can be identified in stool specimens or rectal swabs by EM, ELISA, LA and other immunological techniques for which commercial kits are available. Evidence of rotavirus infection can be demonstrated by serological techniques, but diagnosis is usually based on the demonstration of rotavirus antigen in stools. False-positive ELISA reactions are common in newborns; positive reactions require confirmation by an alternative test.

In both developed and developing countries, rotavirus is associated with about one third of the hospitalized cases of diarrheal illness in infants and young children under 5 years of age. Neonatal rotaviral infections are frequent in certain settings but are usually asymptomatic. Essentially all children are infected by rotavirus in their first 2-3 years of life, with peak incidence of clinical disease in the 6 to 24 month age group. Outbreaks occur among children in day care settings. Rotavirus is more frequently associated with severe diarrhea than other enteric pathogens; in developing countries.

In temperate climates, rotavirus diarrhea occurs in seasonal peaks during cooler months; in tropical climates, cases occur throughout the year, often with a less pronounced peak in the cooler dry months. Infection of adults is usually subclinical, but outbreaks of clinical disease occur in geriatric units. Rotavirus occasionally causes travellers' diarrhea in adults and diarrhea in immunocompromised (including AIDS) patients, parents of children with rotavirus diarrhea and the elderly.

II. EPIDEMIC VIRAL GASTROENTEROPATHY (ICD-10: A08.1)
(Norwalk agent disease, Norwalk-like disease, Viral gastroenteritis in adults, Epidemic Viral gastroenteritis, Acute infectious nonbacterial gastroenteritis, Viral diarrhea, Epidemic diarrhea and vomiting, Winter vomiting disease, Epidemic nausea and vomiting).

Usually a self-limited, mild to moderate disease that often occurs in outbreaks, with clinical symptoms of nausea, vomiting, diarrhea, abdominal pain, myalgia, headache, malaise and low grade fever. GI symptoms characteristically last 24 -48 hours.

The virus may be identified in stool by direct or immune EM or, for the Norwalk virus, by RIA or by reverse transcription polymerase chain reaction (RT-PCR). Serological evidence of infection may be demonstrated by IEM or, for the Norwalk virus, by RIA. Diagnosis requires collection of a large volume of stool, with aliquots stored at 4°C (39°F) for EM, and at –20°C (–4°F) for antigen assays. Acute and convalescent sera (3–4 week interval) are essential to link particles observed by EM with disease etiology. RT-PCR is more sensitive than IEM and can be used to examine links among widely scattered clusters of disease.

Worldwide and common; most often in outbreaks but also sporadically; all age groups are affected. In most developing countries, antibodies are acquired much earlier. Sero-response to Norwalk virus was detected in infants and young children in Bangladesh and Finland.

INFECTIOUS AGENT

I. ROTAVIRAL ENTERITIS: The 70-nm rotavirus belongs to the Reoviridae family. Group A is common, group B is uncommon in infants but has caused large epidemics in adults while group C appears to be uncommon in humans. Groups A, B, C, D, E and F occur in animals. There are 4 major, and at least 10 minor, serotypes of group A human rotavirus, based on antigenic differences in the viral protein 7 (VP7) outer capsid surface protein, the major neutralization antigen. Another outer capsid protein, designated VP4, is associated with virulence and also plays a role in virus neutralization.
II. EPIDEMIC VIRAL GASTROENTEROPATHY: Norwalk-like viruses are small, 27-to 32-nm, structured RNA viruses classified as caliciviruses; it has

been implicated as the most common etiological agent of the nonbacterial gastroenteritis outbreaks. Several morphologically similar but antigenically distinct viruses have been associated with gastroenteritis outbreaks.

RESERVOIR

I. ROTAVIRAL ENTERITIS: Probably humans. The animal viruses do not produce disease in humans; group B and group C rotaviruses identified in humans appear to quite distinct from those found in animals.
II. EPIDEMIC VIRAL GASTROENTEROPATHY: Humans are the only known reservoir.

MODE OF TRANSMISSION

I. ROTAVIRAL ENTERITIS: Probably fecal-oral with possible contact or respiratory spread. Although rotaviruses do not effectively multiply in the respiratory tract, they may be encountered in respiratory secretions. There is some evidence that rotavirus may be present in contaminated water.
II. EPIDEMIC VIRAL GASTROENTEROPATHY: Probably by the fecal-oral route, although contact or airborne transmission from fomites has been suggested to explain the rapid spread in hospital settings. Several outbreaks have strongly suggested primary community foodborne, waterborne and shellfish transmission.

INCUBATION PERIOD

I. ROTAVIRAL ENTERITIS: Approximately 24-72 hours.
II. EPIDEMIC VIRAL GASTROENTEROPATHY: Usually 24-48 hours; in volunteer studies with Norwalk agent, the range was 10 - 50 hours.

PERIOD OF COMMUNICABILITY

I. ROTAVIRAL ENTERITIS: During the acute stage of disease, and later while virus shedding continues. Rotavirus is not usually detectable after about the eighth day of infection, although excretion of virus for 30 days or more has been reported in immunocompromised patients. Symptoms last for an average of 4-6 days.
II. EPIDEMIC VIRAL GASTROENTEROPATHY: During acute stage of disease and up to 48 hours after Norwalk diarrhea stops.

SUSCEPTIBILITY AND RESISTANCE

I. ROTAVIRAL ENTERITIS: Susceptibility is greatest between 6 and 24 month of age. By age 3 years, most individuals have acquired rotavirus antibody. Immunocompromised individuals are at particular risk for prolonged rotavirus antigen excretion and intermittent rotavirus diarrhea. Diarrhea is uncommon in infected infants less than 3 moths of age.
II. EPIDEMIC VIRAL GASTROENTEROPATHY: Susceptibility is widespread. Short-term immunity lasting up to 14 weeks has been demonstrated in volunteers after induced Norwalk illness, but long-term immunity was

variable; some individuals became ill on rechallenge 27-42 months later. Levels of preexisting serum antibody to Norwalk virus did not correlate with susceptibility/resistance.

ACUTE DIARRHOEA

Diarrhea is often accompanied by other clinical signs and symptoms including vomiting, fever, dehydration and electrolyte disturbances. It is a symptom of infection by many different bacterial, viral and parasitic enteric agents. Diarrhea can also occur in association with other infectious diseases such as malaria and measles, as well as chemical agents. Change in the enteric flora induced by antibiotics may produce acute diarrhea by overgrowth and toxin production by *Clostridium difficile.*

Approximately 70%-80% of the vast number of sporadic diarrheal episodes in people visiting treatment facilities in less developed countries could be diagnosed etiologically if the complete battery of newer laboratory tests were available and utilized.

From a practical clinical standpoint, diarrheal illnesses can be divided into six clinical presentations:

1. Simple diarrhea, managed by oral rehydration with solutions containing water, glucose and electrolytes, with its specific etiology not important in management;
2. Bloody diarrhea (dysentery), caused by organisms such as *Shigella, E. coli O157:H7* and certain other organisms;
3. Persistent diarrhea that lasts at least 14 days;
4. Severe purging as seen in cholera;
5. Minimal diarrhea, associated with vomiting, typical of some viral gastroenteritides; and illness from the toxins, such as those of *Staphylococcus aureus, Bacillus cereus or Cl.perfringens;* and
6. Hemorrhagic colitis, with watery diarrhea containing gross blood but without fever or fecal leukocytes.

Diarrhea caused by Escherichia coli

Strains of *Escherichia coli* that cause diarrhea are of six major categories:
1) Enterohemorrhagic; 2) enterotoxigenic; 3) enteroinvasive; 4) enteropathogenic; 5) enteroaggregative; and 6) diffuse-adherent.
Each category has a different pathogenesis, possesses distinct virulence properties, and comprises a separate set of O:H serotypes. Differing clinical syndromes and epidemiological patterns may also be seen.

IDENTIFICATION

I. DIARRHEA CAUSED BY ENTEROHEMORRHAGIC STRAINS (ICD-10: A04.3)
(EHEC, Shiga toxin producing *E. coli* [STEC], *E. coli 0*157:H7, Verotoxin production *E. coli)* [VTEC]

The diarrhea may range from mild and nonbloody to stools that are virtually all blood but contain no fecal leukocytes. The most feared clinical manifestations of EHEC infection are the hemolytic uremic syndrome (HUS) and thrombotic thrombocytopenic purpura (TTP). Approximately 2–7% of subjects who manifest EHEC diarrhea progress to develop hemolytic uremic syndrome (HUS).

EHEC elaborate potent cytotoxins called Shiga toxins 1 and 2. Shiga toxin 1 is identical to Shiga toxin elaborated by *Shigella dysenteriae* 1; notably, HUS is also a well-recognized severe complication of *S. dysenteriae* 1 disease. Previously, these toxins were called verotoxins 1 and 2 or Shiga-like toxins 1 and 2. Elaboration of these toxins depends on the presence of certain phages carried by the bacteria. In addition, EHEC strains harbor a virulence plasmid that is involved in attachment of the bacteria to intestinal mucosa. Most EHEC strains have within their chromosome a pathogenicity island that contains multiple virulence genes encoding proteins that cause attaching and effacing lesions of the human intestinal mucosa. Lack of fever in most patients can help to differentiate this from shigellosis and dysentery caused by enteroinvasive strains of *E. coli* or by *Campylobacter.*

These infections are now recognized to be an important problem in North America, Europe, South Africa, Japan, the southern cone of South America and Australia. Their relative importance in the rest of the world is less well established. Serious outbreaks, including cases of hemorrhagic colitis, HUS and some deaths, have occurred from inadequately cooked hamburgers, unpasteurized milk, apple cider (made from apples that were probably contaminated by cow manure).

II. DIARRHEA CAUSED BY ENTEROTOXIGENIC STRAINS (ETEC), (ICD-10:AO4.1)
A major cause of travelers' diarrhea in people from industrialized countries who visit less developed countries. This bacterial disease is also an important cause of dehydrating diarrhea in infants and children in less developed countries. Enterotoxigenic strains may behave like *Vibrio cholerae* in producing profuse watery diarrhea without blood or mucus. Abdominal cramping, vomiting, acidosis, prostration and dehydration can occur, and low-grade fever may or may not be present; the symptoms usually last fewer than 5 days.

ETEC can be identified by demonstrating enterotoxin production, by immunoassays, bioassays or by DNA probe techniques that identify LT and ST genes (for heat labile and heat stable toxins) in colony blots.

It is an infection primarily of developing countries. During the first 3 years of life, children in developing countries experience multiple ETEC infections, which leads to the acquisition of immunity; consequently, illness in older children and adults occurs less frequently. Infection occurs among travelers from industrialized countries that visit less-developed countries.

III DIARRHEA CAUSED BY ENTEROINVASIVE STRAINS (EIEC) (ICD-10: A04.2)

This inflammatory disease of the gut mucosa and submucosa caused by EIEC strains of *E.coli* closely resembles that produced by *Shigella*. The organisms possess the same plasmid dependent ability to invade and multiply within epithelial cells. However, clinically, the syndrome of watery diarrhea due to EIEC is much more common than dysentery. The O antigens of EIEC may cross-react with *Shigella* O antigens. Illness begins with severe abdominal cramps, malaise, watery stools, tenesmus and fever; in less than 10% of patients, it progresses to the passage of multiple, scanty, fluid stools containing blood and mucus.

EIEC may be suspected by the presence of many fecal leukocytes visible in a stained smear of mucus, a finding also in shigellosis. An immunoassay test that detects the plasmid encoded specific outer membrane proteins that are associated with epithelial cell invasiveness; a bioassay (the guinea pig-keratoconjunctivitis test) detects epithelial cell invasiveness; DNA probes detect the enteroinvasiveness plasmid.

EIEC infections are endemic in less developed countries, and cause about 1-5% of diarrheal episodes among people visiting treatment centres. Occasional infections and outbreaks of EIEC diarrhea have been reported in industrialized countries.

IV DIARRHEA CAUSED BY ENTEROPATHOGENIC STRAINS (ICD-10: A04.0)

(EPEC, Enteropathogenic *E. coli* enteritis)

This is the oldest recognized category of diarrhea producing *E. coli.* implicated in 1940s and 1950s studies in which certain O:H serotypes were found to be associated with infant summer diarrhea, outbreaks of diarrhea in infant nurseries, and community epidemics of infant diarrhea. Diarrheal disease in this category is virtually confined to infants less than 1 year of age in whom it causes watery diarrhea with mucus, fever and dehydration. EPEC cause dissolution of the microvilli of enterocytes and initiate attachment of the bacteria to enterocytes. The diarrhea in infants can be both severe and

prolonged, and in developing countries may be associated with high case-fatality.

EPEC can be tentatively identified by agglutination with antisera that detect EPEC O serogroups, but confirmation requires both O and H typing with high quality reagents. EPEC organisms exhibit HEp-2 cells in cell cultures, a property that requires the presence of an EPEC virulence plasmid. The EPEC adherence factor (EAF) DNA probe detects the EPEC virulence plasmid; there is a 98% correlation between the detection of localized adherence and EAF probe positivity.

Since the late 1960s, EPEC has largely disappeared at an important cause of infant diarrhea in North America and Europe. However, it remains a major agent of infant diarrhea in many developing areas, including Asia.

V. DIARRHEA CAUSED BY ENTEROAGGREGATIVE *E.COLI* (EAggEC) (ICD-10: A04.4)

This category of diarrhea producing *E. coli* is an important cause of infant diarrhea in less developed countries where it is the single most common cause of persistent diarrhea in infants. In animal models, these *E. coli* organisms evoke a characteristic histopathology in which EAggEC adhere to enterocytes in thick biofilm of aggregating bacteria and mucus. At present, the most widely available method to identify EAggEC is by the HEp-2 assay.

This category of diarrhea producing *E. coli* was first associated with infant diarrhea in a study in Chile in the late 1980s. It was subsequently recognized in developing countries as being particularly associated with persistent diarrhea (diarrhea that continues unabated for at least 14 days), an observation that has since been confirmed by reports form Brazil, Mexico and Bangladesh.

Reports associating EAggEC with infant diarrhea, and particularly persistent diarrhea, has come from multiple countries in Latin America, Asia and Africa. Reports suggest that EAggEC may be responsible for a small proportion of diarrheal disease in industrialized countries as well.

VI. DIARRHEA CAUSED BY DIFFUSE - ADHERENCE *E.COLI* (DAEC) (ICD-10: A04.4)

A sixth category of diarrhea producing *E. coli* now recognized is diffuse adherence *E. coli* (DAEC). The name derives from the characteristic pattern of adherence of these bacteria to HEP-2 cells in tissue culture. DAEC is the least well-defined category of diarrhea causing *E. coli*. Nevertheless, data from several epidemiological field studies of pediatric diarrhea in less developed countries have found DAEC to be significantly more common in children with diarrhea than in matched controls; other studies have failed to find such a difference. Notably, preliminary evidence suggests that DAEC may be more

pathogenic in children of preschool age rather than in infants and toddlers. Two DAEC strains failed to cause diarrhea when fed to volunteers and no outbreaks due to this category have yet been recognized. At present little is known about the reservoir, modes of transmission, and host risk factors or period of communicability of DAEC.

INFECTIOUS AGENT

I. DIARRHEA CAUSED BY ENTEROHEMORRHAGIC STRAINS (EHEC)
While the main EHEC serotype is *E. coli* O157:H7, other serotypes such as O26:H11, O111:H8, O103:H2, O113:H21, and O104:H21 have been implicated.

II. DIARRHEA CAUSED BY ENTEROTOXIGENIC STRAINS (ETEC)
ETEC elaborate a heat labile enterotoxin (LT), a heat stable toxin (ST) or both toxins (LT/ST). The most common O serogroups include O6, O8, O15, O20, O25, O27, O63, O78, O80, O114, O115, O128ac, O148, O153, O159 and O167.

III. DIARRHEA CAUSED BY ENTEROINVASIVE STRAINS (EIEC)
Strains of *E. coli* shown to possess enteroinvasiveness dependent on the presence of a larger virulence plasmid encoding invasion plasmid antigens. The main O serogroups in which EIEC fall includes O28ac, O29, O112, O124, O136, O143, O144, O152, O164 and O167.

IV. DIARRHEA CAUSED BY ENTEROPATHOGENIC STRAINS
(EPEC, Enteropathogenic *E. coli* enteritis)
The major EPEC O serogroups include O55, O86, O111, O119, O125, O126, O127, O128ab and O142.

V. DIARRHEA CAUSED BY ENTEROAGGREGATIVE *E.COLI* (EAggEC)
EAggEC harbour a virulence plasmid required for expression of the unique fimbriae that encode aggregative adherence and many strains express a cytotoxin/enterotoxin. Among the most common EAggEC O serotypes and O3:H2 are O44:H18. Many EAggEC strains initially appear as rough strains lacking O antigens.

RESERVOIR

Cattle are the most important reservoir of EHEC (Diarrhea caused by Enterohemorrhagic strains); humans may also serve as a reservoir for person-to-person transmission.

Humans are the reservoir of etec (diarrhea caused by enterotoxigenic strains). etec infections are largely species specific; people constitute the reservoir for strains causing diarrhea in humans.

Humans are the reservoir of EIEC (Diarrhea caused by Enteroinvasive strains) and EPEC (Diarrhea caused by Enteropathogenic strains).

MODE OF TRANSMISSION

I. DIARRHEA CAUSED BY ENTEROHEMORRHAGIC STRAINS

Transmission occurs mainly by ingestion of contaminated food; as with *Salmonella,* it is most often due to inadequately cooked beef (especially ground beef) and also raw milk and fruit or vegetables contaminated with ruminant feces. As with *Shigella,* transmission also occurs directly from person-to-person, in families, childcare centres and custodial institutions. Waterborne transmission has also been documented; one outbreak was associated with swimming in a crowded lake and one was caused by drinking contaminated unchlorinated municipal water.

II. DIARRHEA CAUSED BY ENTEROTOXIGENIC STRAINS (ETEC)
Contaminated food and, less often, contaminated water. Transmission via contaminated weaning foods may be particularly important in infection of infants. Direct contact transmission by fecally contaminated hands is believed to be rare.

III DIARRHEA CAUSED BY ENTEROINVASIVE STRAINS (EIEC)
Scant available evidence suggests that EIEC is transmitted by contaminated food.

IV DIARRHEA CAUSED BY ENTEROPATHOGENIC STRAINS (EPEC)
By contaminated infant formula and weaning foods. In infant nurseries, transmission by fomites and by contaminated hands can occur if handwashing techniques are compromised.

INCUBATION PERIOD

I. DIARRHEA CAUSED BY ENTEROHEMORRHAGIC STRAINS (EHEC): Typically relatively long, ranging from 2 to 8 days, with a median of 3 - 4 days.

II. DIARRHEA CAUSED BY ENTEROTOXIGENIC STRAINS (ETEC): Incubations as short as 10 - 12 hours have been observed in outbreaks and in volunteer studies with certain LT-only and ST-only strains. The incubation of LT/ST diarrhea in volunteer studies has usually been 24-72 hours.

III DIARRHEA CAUSED BY ENTEROINVASIVE STRAINS (EIEC): Incubations as short as 10 and 18 hours have been observed in volunteer studies and outbreaks, respectively.

IV DIARRHEA CAUSED BY ENTEROPATHOGENIC STRAINS (EPEC): As short as 9 -12 hours in adult volunteer studies. It is not known whether the same incubation applies to infants who acquire infection by natural transmission.

V. DIARRHEA CAUSED BY ENTEROAGGREGATIVE *E.COLI* (EAggEC): The incubation period is estimated to be 20 -48 hours.

PERIOD OF COMMUNICABILITY

I. DIARRHEA CAUSED BY ENTEROHEMORRHAGIC STRAINS (EHEC): The duration of excretion of the pathogen, which is typically for a week or less in adults but 3 weeks in one third of children. Prolonged carriage is uncommon.

II. DIARRHEA CAUSED BY ENTEROTOXIGENIC STRAINS (ETEC): For the duration of excretion of the pathogenic ETEC, which may be prolonged.
III DIARRHEA CAUSED BY ENTEROINVASIVE STRAINS (EIEC): Duration of excretion of EIEC strains
IV DIARRHEA CAUSED BY ENTEROPATHOGENIC STRAINS (EPEC): Limited to the duration of excretion of EPEC, which may be prolonged.

SUSCEPTIBILITY AND RESISTANCE

I. DIARRHEA CAUSED BY ENTEROHEMORRHAGIC STRAINS (EHEC): The infectious dose is very low. Little is known about difference in susceptibility and immunity. Old age appears to be a risk factor, so hypochlorhydria may be a factor contributing to susceptibility. Children less than 5 years of age are at greatest risk of developing HUS.
II. DIARRHEA CAUSED BY ENTEROTOXIGENIC STRAINS (ETEC): Epidemiological studies and rechallenge studies in volunteers clearly demonstrate that serotype specific immunity is acquired following ETEC infection. Multiple infections with different serotypes are required to develop broad-spectrum immunity against ETEC.
III DIARRHEA CAUSED BY ENTEROINVASIVE STRAINS (EIEC): Little is known about susceptibility and immunity to EIEC.
IV DIARRHEA CAUSED BY ENTEROPATHOGENIC STRAINS (EPEC): Although susceptibility to clinical infection appears to be confined virtually to young infants in nature, diarrhea can be induced experimentally in some adult volunteers, specific immunity may be important in determining susceptibility. EPEC infection is uncommon in breast fed infants.

RATIONALE FOR SURVEILLANCE

In Nepal diarrhoeal diseases are one of the major causes of deaths and malnutrition. Within first 60 months of her/his life he/she experiences 2.3 episodes per year resulting in about 30,000 deaths annually. In addition to that these repeated attacks of diarrhoea are a major cause of malnutrition and faltering height and weight and malnourished children also suffer more severe attack of diarrhoea and hence higher mortality in this country.

RECOMMENDED CASE DEFINITION

Clinical case definition

Acute watery diarrhoea (passage of 3 or more loose or watery stools in the past 24 hours) with or without dehydration.

Laboratory criteria for diagnosis

Laboratory culture of stools may be used to confirm possible outbreaks of specific agents, but is not necessary for case definition.

- Demonstration of specific antigen of possible pathogen by rapid diagnostic test kit
- Isolation, identification and characterization of causative agent

- Detection of possible pathogen by IFA, ELISA
- Detection of pathogen by PCR assay

Case classification
Not applicable

RECOMMENDED TYPES OF SURVEILLANCE FOR SENTINEL SITES

- Patient records should be maintained at Hospital level in each EWARS sentinel sites.
- Medical Recorders of EWARS sentinel sites should be maintained EWARS-1 register by recording of all clinical cases of Acute Diarrhoeal Diseases (including Gastroenteritis) after consulting the case investigation forms, Emergency register, Inpatient/OPD register and other concerns registers.
- Medical Recorders of EWARS sentinel sites should reporting on all clinical cases including zero reports of Acute Diarrhoeal Diseases (including Gastroenteritis) in the weekly EWARS reporting from (EWARS-3).
- Medical Recorders of EWARS sentinel sites must reporting on immediate reporting forms (EWARS-2), when the observed number of cases exceeds the expected number of cases or more than 5 cases from a same geographical area are admitted.
- Nursing In charge should be informed to Medical Recorder about the acute diarrhoeal cases admitted in any wards.
- Lab personnel should be informed to Medical recorder about the laboratory confirmation of the pathogen.
- All outbreaks (clinical cases) should be reported immediately to the respective DHO/DPHO, Regional Health Services Directorate and the EDCD/DHS for immediate investigation and, if possible, laboratory confirmation.

RECOMMENDED MINIMUM DATA ELEMENTS

As per EWARS reporting forms and guidelines.

PRINCIPAL USES OF DATA FOR ACTION

- Monitor trends in diseases incidence.
- Detect possible outbreak and rapid response at the local level.
- Identify high-risk areas for further targeting of intervention.
- Estimate incidence rate and case-fatality rate.
- Estimate the incidence, attack, and case-fatality rate during outbreak situation.
- Undertake appropriately timed investigations and assess the spread and progress of the disease

- Support plan for the distribution of medical supplies/logistics (diagnostic test, antibiotics etc.) and allocation of control teams.
- Determine the effectiveness of control measures.

SPECIFIC TREATMENT

Aggressive rehydration by oral and intravenous routes to repair fluid and electrolyte deficits and to replace the prodigious ongoing diarrhoeal losses is the cornerstone of diarrhoea therapy. As rehydration therapy becomes increasingly effective, patients who survive from hypovolemic shock and severe dehydration manifest certain complications such as hypoglycemia that must be recognized and treated promptly.

In initiating prompt agressive fluid therapy with volumes of electrolyte solution adequate to correct dehydration, acidosis and hypokalemia most patients with mild or moderate fluid loss can be treated entirely with oral rehydration using solutions that contain glucose 20 g/L (or sucrose 40 g/L or cooked rice powder 50 g/L); NaCI (3.5g/L); KCI (1.5 g/L) and trisodium citrate dihydrate (2.9 g/L) or $HaHCO_3$ (2.5 g/L). Mild and moderate volume depletion should be corrected with oral solutions by replacing, over 4-6 hours, a volume matching the estimated fluid loss (approximately 5% of body weight for mild and 7% for moderate dehydration). Continuing losses are replaced by giving, over 4 hours, a volume of oral solution 1.5 times the stool volume lost in the previous 4 hours.

Patients in shock should be given rapid IV rehydration with a balanced multielectrolyte solution containing approximately 130 mEq/L of Na^+, 25-48 mEq/L of bicarbonate, acetate or lactate ions, and 10-15 mEq/L of K^+. Useful solutions include Ringer's lactate or WHO "diarrhea treatment solution" (4 g NaCI, 1 g KCI, 6.5 g sodium acetate and 8 g glucose/L), and "Dacca solution" (5 g NaCI, 4 g $NaHCO_3$ and 1 g KCI/L), which can be prepared locally in an emergency. The initial fluid replacement should be 30 ml/kg in the first hour for infants and in the first 30 minutes for persons over 1 year of age, after which the patient should be reassessed. After circulatory collapse has been effectively eversed, most patients can be switched to oral rehydration to complete the 10% initial fluid deficit replacement and to match continuing fluid loss.

I. DIARRHEA CAUSED BY ENTEROHEMORRHAGIC STRAINS (EHEC): Fluid and electrolyte replacement is important when diarrhea is watery or there are signs of dehydration. The role of antibacterial treatment of infections with *E. coli O157:H7* and other EHEC is uncertain. Some evidence suggests that treatment with TMP+SMX fluoroquinolones and certain other antimicrobials may precipitate complications such as HUS.

II. DIARRHEA CAUSED BY ENTEROTOXIGENIC STRAINS (ETEC): Electrolyte-fluid therapy to prevent or treat dehydration is the most important measure (see Cholera, section 9B7). Most cases do not require any other

therapy. For severe travelers' diarrhea in adults, early treatment with loperamide (not for children) and an antibiotic such as a fluoroquinolone (ciprofloxacin PO 500 mg twice daily) or norfloxacin (PO 400 mg daily) is given for 5 days. Fluoroquinolones are used as initial therapy because many ETEC strains worldwide are resistant to a variety of other antimicrobials. However, if local strains are known to be sensitive, TMP-SMX (PO) (160 mg-800 mg) twice daily or doxycycline (PO) (100 mg) once daily, for 5 days are useful. Feeding should be continued, according to the patient's appetite.

III. DIARRHEA CAUSED BY ENTEROPATHOGENIC STRAINS: Electrolyte-fluid therapy (oral or IV) is the most important measure. Most cases do not require any other therapy. For severe enteropathogenic infant diarrhea, oral TMP-SMX (10-50 mg/kg/day) has been shown to ameliorate the severity and duration of diarrheal illness; it should be administered in 3 - 4 divided doses for 5 days. However, since many EPEC strains are resistant to a variety of antibiotics, selection should be based on the sensitivity of local isolated strains. Feeding, including breast-feeding, should be continued.

IV. ROTAVIRAL ENTERITIS: None. Oral rehydration therapy with oral glucose–electrolyte solution is adequate in most cases. Parenteral fluids are needed in cases with vascular collapse or uncontrolled vomiting (see cholera). Antibiotics and antimotility drugs are contraindicated.

V. EPIDEMIC VIRAL GASTROENTEROPATHY: Fluid and electrolyte replacement in severe cases.

VIBRIO CHOLERAE

(ICD-10: A00)

IDENTIFICATION

Vibrio Cholerae is an acute bacterial enteric disease characterized in its severe form by sudden onset, profuse painless watery stools, nausea and vomiting early in the course of illness, and, in untreated cases, rapid dehydration, acidosis, circulatory collapse, hypoglycemia in children, and renal failure. Asymptomatic infection is much more frequent than clinical illness, especially with organisms of the El Tor biotype; mild cases with only diarrhea are common, particularly among children. In severe untreated cases (cholera gravis), death may occur within a few hours, and the case-fatality rate may exceed 50%; with proper treatment, the rate is less than 1%.

Diagnosis is confirmed by isolating *Vibrio cholerae* of the serogroup O1 or O139 from feces. If laboratory facilities are not nearby or immediately available, Cary Blair transport medium can be used to transport a fecal or rectal swab. For clinical purposes, a quick presumptive diagnosis can be made by dark field or phase microscopic visualization of the vibrios moving like "shooting stars," inhibited by preservative free, serotype specific antiserum. For epidemiologic purposes, a presumptive diagnosis can be based on the demonstration of a significant rise in titer of antitoxic and vibriocidal antibodies. In nonendemic areas, isolated organisms from initial suspected cases should be confirmed by appropriate biochemical and serologic reactions and by testing the organisms for cholera toxin production or for the presence of cholera toxin genes. In epidemics, once laboratory confirmation and antibiotic sensitivity have been established, all cases need not be laboratory confirmed.

The new serogroup, designated O139 Bengal, spread rapidly throughout the region over the next few months affecting several hundred thousand persons. During this epidemic period, *V. cholerae* O139 almost completely replaced *V. cholerae* O1 strain in hospitalized cholera patients and in samples of surface water. Cholera O139 may in the future cause large explosive epidemics in another region of the world and therefore requires continued international surveillance.

INFECTIOUS AGENT

Vibrio cholerae serogroup O1 includes two biotypes-classical and El Tor-each of which includes organisms of Inaba, Ogawa and rarely Hikojima serotypes. The clinical pictures of illness caused by *V. cholerae* O1 of either biotype and *V. cholerae* O139 are similar because an almost identical enterotoxin is elaborated by these organisms. In any single epidemic, one particular type tends to be dominant; currently the El Tor biotype is predominant.

RESERVOIR

Humans; observations over the past two decades have clearly demonstrated that environmental reservoirs exist.

MODE OF TRANSMISSION

Through ingestion of food or water contaminated directly or indirectly with feces or vomitus of infected persons. El Tor and O139 organisms can persist in water for long periods. When epidemic cholera appeared in Kathmandu valley in explosive fashion in 2007-08, faulty municipal water systems, contaminated surface waters, and unsafe domestic water storage methods resulted in extensive waterborne transmission of cholera. Beverages prepared with contaminated water and sold by street vendors, ice and even commercial bottled water were incriminated. Cooked grains with sauces have been incriminated as vehicles in cholera transmission. *V. cholerae* introduced by a food handler into one of these foods and stored unrefrigerated can increase by several logs within 8-12 hours. Vegetables and fruit "freshened" with untreated sewage wastewater have also served as vehicles of transmission.

INCUBATION PERIOD

From a few hours to 5 days, usually 2-3 days.

PERIOD OF COMMUNICABILITY

Presumably as long as stools are positive, usually only a few days after recovery. Occasionally the carrier state may persist for several months. Antibiotics known to be effective against the infecting strains (e.g., tetracycline against the 0139 strain and most 01 strains) shorten the period of communicability.

SUSCEPTIBILITY AND RESISTANCE

Variable; gastric achlorhydria increases risk of illness, and breast fed infants are protected. Cholera gravis due to the *EI Tor* biotype and O139 vibrio occurs significantly more often among persons with blood group O. Infection with either *V. cholerae* O1 or O139 results in a rise in agglutinating and antitoxic antibodies, and increased resistance to reinfection. Serum vibriocidal antibodies, which are readily detected following 01 infection (but for which comparably specific, sensitive and reliable assays are not available for O139 infection), are the best immunologic correlate of protection against O1 cholera. Field studies show that an initial clinical infection by *V. cholera* O1 of the classical biotype confers protection against either classical or El Tor biotypes; in contrast an initial clinical infection caused by biotype El Tor results in only a modest level of long-term protection that is limited to El Tor infections. In endemic areas, most people acquire antibodies by early adulthood. However, infection with O1 strains affords no protection against O139 infection and vice versa.

RATIONALE FOR SURVEILLANCE

In world, Cholera causes an estimated 120, 000 deaths per year and is prevalent in 80 countries. The world is currently experiencing the 7th pandemic. In Nepal, Cholera is an endemic disease. The number of Cholera cases starts to increase with the rise in temperature (April/May) and reaches maximum during the monsoon season (July). Although the majority of isolates of *V. Cholera* in Nepal have been due to the serogroup O1 *(Ogawa),* cases of *V. Cholera* serogroup O139 has also been reported. This serogroup is also responsible for large scale epidemics of severe dehydrating diarrhoea. However no deaths from cholera were reported in those years. The number of reported cases represents only a small proportion of the total number of cases. Refugee or displaced populations are at major risk of epidemics due to the conditions prevailing in the camps (unsafe water, poor sanitation and hygiene). Control of disease requires appropriate surveillance with universal case reporting. Health education of the population at risk and improvement of living conditions are essential preventive measures.

RECOMMENDED CASE DEFINITION

Clinical case definition

- Acute watery diarrhoea, with or without vomiting in a patient aged 3 years or more*

Laboratory criteria for diagnosis

Isolation of *vibrio cholerae* O1 or O139 from stools in any patient with acute diarrhoea.

Note: The NPHL (Teku, Kathmandu) act as Reference laboratories in the country for species identification.

Case classifications

Suspected: A case that meets the clinical case definition

Probable: Not applicable

Confirmed: A suspected case that is laboratory-confirmed.

** Cholera does appear in children under 3 years; however, the inclusion of all cases of acute watery diarrhea in the 2-3 year age group in the reporting of cholera greatly reduces the specificity of reporting. For management of cases of acute watery diarrhoea in an area where there is a cholera epidemic, cholera should be suspected in all patients with acute watery diarrhoea.*

RECOMMENDED TYPES OF SURVEILLANCE FOR SENTINEL SITES

- Patient records should be maintained at Hospital level in each EWARS sentinel sites.
- Medical Recorders of EWARS sentinel sites should be maintained EWARS-1 register by recording of all confirmed cases of Cholera after consulting the Emergency register, Inpatient/OPD register, Laboratory register and other concerns registers.

- Medical Recorders of EWARS sentinel sites must report on immediate reporting forms (EWARS-2), if any case of cholera is laboratory confirmed.
- Medical Recorders of EWARS sentinel sites should reporting on all cases including zero reports of Cholera in the weekly EWARS reporting from (EWARS-3).
- Nursing In-charge should be informed to Medical Recorder about the cholera cases admitted in any wards.
- Lab personnel should be informed to Medical recorder about the laboratory confirmation of the pathogen.
- All outbreaks (clinical cases) should be reported immediately to the respective DHO/DPHO, Regional Health Services Directorate and the EDCD/DHS for immediate investigation and, if possible, laboratory confirmation.

RECOMMENDED MINIMUM DATA

As per EWARS reporting forms and guidelines.

PRINCIPAL USES OF DATA FOR ACTION

- Detect outbreaks
- Estimate the incidence, attack, and case-fatality rate during outbreak situation
- Undertake appropriately timed investigations
- Assess the spread and progress of the disease
- Plan for treatment, supplies (logistics), prevention and control measures
- Determine the effectiveness of control measures

SPECIFIC TREATMENT

These are three mainstays in the treatment of patients with cholera: (1) aggressive rehydration therapy; (2) administration of effective antibiotics; and (3) treatment of complications. Aggressive rehydration by oral and intravenous routes to repair fluid and electrolyte deficits and to replace the prodigious ongoing diarrheal losses is the cornerstone of cholera therapy. Appropriate antimicrobials are an important adjunct to fluid therapy, as they diminish the volume and duration of purging and rapidly curtail the excretion of *vibrios*, thereby diminishing the chance of secondary transmission. Finally, as rehydration therapy becomes increasingly effective, patients who survive from hypovolemic shock and severe dehydration manifest certain complications such as hypoglycemia that must be recognized and treated promptly. If these basic guidelines are adhered to, case fatality, even during explosive outbreaks can be kept to less than 1%.

In initiating prompt aggressive fluid therapy with volumes of electrolyte solution adequate to correct dehydration, acidosis and hypokalemia most patients with mild or moderate fluid loss can be treated entirely with oral rehydration using solutions

that contain glucose 20 g/L; NaCl (3.5g/L); KCl (1.5 g/L); and trisodium citrate dihydrate (2.9 g/L) or $HaHCO_3$(2.5 g/L). Mild and moderate volume depletion should be corrected with oral solutions by replacing, over 4-6 hours, a volume matching the estimated fluid loss (approximately 5% of body weight for mild and 7% for moderate dehydration). Continuing losses are replaced by giving, over 4 hours, a volume of oral solution 1.5 times the stool volume lost in the previous 4 hours.

Patients in shock should be given rapid IV rehydration with a balanced multielectrolyte solution containing approximately 130 mEq/L of Na^+, 25-48 mEq/L of bicarbonate, acetate or lactate ions, and 10-15 mEq/L of K^+. Useful solutions include Ringer's lactate or WHO "diarrhea treatment solution" (4 g NaCl, 1 g KCl, 6.5 g sodium acetate and 8 g glucose/L), and "Dacca solution" (5 g NaCl, 4 g $NaHCO_3$ and 1 g KCl/L), which can be prepared locally in an emergency. The initial fluid replacement should be 30 ml/kg in the first hour for infants and in the first 30 minutes for persons over 1 year of age, after which the patient should be reassessed. After circulatory collapse has been effectively reversed, most patients can be switched to oral rehydration to complete the 10% initial fluid deficit replacement and to match continuing fluid loss.

Appropriate antimicrobial agents can shorten the duration of diarrhea, reduce the volume of rehydration solutions required, and shorten the duration of *vibrio* excretion. Adults are given tetracycline 500 mg 4 times a day, and children 12.5 mg/kg 4 times daily, for 3 days. When tetracycline resistant strains of *v. cholerae* are prevalent, alternative antimicrobial regimens include TMP-SMX (320 mg trimethoprim and 1600 mg sulfamethoxazole twice daily for adults and 8 mg/kg trimethoprim and 40 mg/kg sulfamethoxazole daily in 2 divided doses for children, for 3 days); furazolidone (100 mg 4 times daily for adults and 1.25 mg/ kg 4 times daily for children, for 3 days); or erythromycin (250 mg 4 times daily for adults and 10 mg/kg 3 times daily for children, for 3 days). Ciprofloxacin, 250 mg once daily for three days, is also a useful regimen for adults. *V. cholerae* O139 strains are resistant to TMP-SMX. Since individual strains of *V. cholerae* O1 or O139 may be resistant to any of these antimicrobials, knowledge of the sensitivity of local strains to these agents, if available, should be used to guide the choice of the antimicrobial therapy.

SEVERE ACUTE RESPIRATORY INFECTION

Surveillance for Human AI ILI / SARI

Objectives of an influenza surveillance system

1. Detect unusual or unexpected viral respiratory outbreaks.
2. Determine the epidemiologic characteristics of influenza and other viral respiratory diseases (caused by, for example, Adenovirus, Para-influenza, and Respiratory syncytial Virus).
3. Monitor influenza viruses and make recommendations for annual vaccine composition, determine the concordance between the vaccine and currently circulating strains; detect, in a timely manner, the appearance of new subtypes.
4. Estimate the burden of ILI and SARI in humans.
5. Guide the development of policies and guidelines for influenza prevention and control.
6. Build the foundation of future studies on the impact of disease prevention and control interventions.

Sentinel surveillance for human Influenza: Achieved through:

- **Outpatient clinic** based Influenza like illness (ILI cases) or
- **Admitted cases** of severe acute respiratory illness (SARI cases)

A simple passive surveillance system to tract influenza episodes in the population with an objective to be able to detect any unusual activity as well as to keep tract of types of organisms causing respiratory illness in the communities.

Enhanced surveillance for human influenza A/H5: It involves active and passive approaches to find influenza cases with history of exposure through contact tracing in the area where case patients reside or where bird /animal outbreaks of Influenza A/H5 are occurring. It can include measures such as telephone hotlines, media, radio or other emergency networks as needed for getting reports about suspect cases in the community.

Influenza Like illness (ILI):

- ILI surveillance is a syndromic surveillance system. It is not a illness by itself rather it is a group of several illnesses that have a similar initial presentation while cases are been seen in the outpatient clinics and ambulatory settings.
- Evidence based studies have shown that ILI illnesses data closely correlates with the laboratory based data from Influenza surveillance programs and also helps in the early detection of any impending epidemic. Yearly, adults and children can average one to three and three to six ILI, respectively in USA.

Severe acute Respiratory Infection (SARI):

- Also is a syndromic presentation like ILI, however with some more complications like involvement of lower respiratory tract, Pneumonia,

development of respiratory distress and thereby causing a need for admission to the hospital facility.

RECOMMENDED CASE DEFINITION

Influenza Like illness (ILI):

- A case with: Sudden onset of a fever over 38°C

AND
- Cough or sore throat

AND
- An absence of other diagnoses.

Severe acute Respiratory Infection (SARI):

- A case with: Sudden onset of fever over 38°C

AND
- Cough or sore throat

AND
- Shortness of breath or difficulty breathing

AND
- Requiring hospital admission

Present status of ILI reporting in Nepal and proposed reporting system

- ILI is not a clinical diagnosis and is not recorded by any doctor in the OPD
- ILI cases are too many and overburden the EWARS reporting system
- Present ILI reports from sentinel sites are inconsistent
- What presently is being reported under the name of ILI by EWARS sentinel sites in Nepal is actually SARI cases
- It is proposed to start SARI surveillance with weekly case reporting under EWARS
- Doctors will be trained to ask history of exposure form all ILI / SARI cases

Suspected case of Human AI

- A person presenting with unexplained acute lower respiratory illness with fever (>38 ºC) and cough, shortness of breath or difficulty breathing.

  and
- One or more of the following epidemiological linkage or exposures in the 14 days prior to onset of the symptoms:
  - **Close contact** (< 1 m) with a person who is a suspected, probable, or confirmed **H5N1**
  - **Exposure to** poultry or wild birds or animals or their remains or to environments contaminated by their faeces in an area where **H5N1**

infections in animals or humans have been suspected or confirmed in the last month

- **Consumption** of raw or undercooked poultry products in an area where **H5N1** infections in animals or humans have been suspected or confirmed in the last month
- **Travel to**: an area where **H5N1** infections in animals or humans have been suspected or confirmed in the last one month
- **Handling samples** (animal or human) suspected of containing **H5N1** virus in a laboratory or other setting

Person Under Investigation (PUI) for HAI

- A person whom public health authorities have decided to investigate for possible HAI A /H5 infection.

Or

- A case with SARI like symptoms

And has one of the following histories of exposure:

- **Belongs to one of the "high risk categories**"
- **Had close contact with** (in the 14 days prior to onset of the symptoms):
- Sick/dead poultry or birds; or
- Direct contact (within 1 meter) with hospitalized patients who have (or died of) severe respiratory illness.

High Risk Groups

- Children playing with or taking care of infected poultry and/or asymptomatic infected ducks
- Poultry handlers in live animal markets / wet markets
- Cullers without using proper PPE precautions
- Persons involved in defeathering and preparing of sick birds in wet markets / backyard poultry / kitchens
- People consuming undercooked poultry products
- Hospital functionaries managing human cases of AI without using proper PPE precautions
- Veterinarians exposed to avian influenza infected poultry
- Human or animal laboratory personnel or other staff who handle animal or human samples from persons / patients suspected of or known to contain H5N1 virus in a laboratory or field setting

Probable case for HAI

- **Probable Case Definition 1:** A person meeting the criteria for a suspected case AND meets one of the following additional criteria:
    - Infiltrates or evidence of an acute pneumonia on chest radiograph plus evidence of respiratory failure (hypoxemia, severe tachypnoea) Or

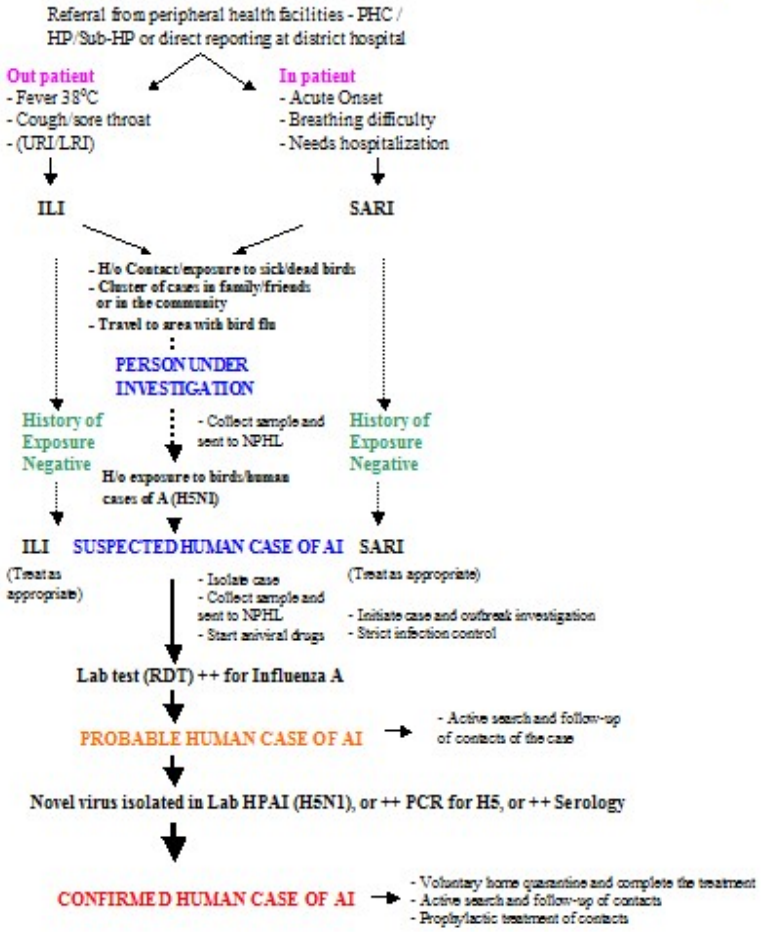
- Positive laboratory confirmation of influenza A infection but insufficient laboratory evidence for A (H5N1) infection

- **Probable definition 2**:
  - A person dying of an unexplained acute respiratory illness who is considered to be epidemiologically linked by time, place, and exposure to a probable or confirmed H5N1 case

Confirmed case of HAI

- A person meeting the criteria for a suspected or probable case AND meets one of the following positive results at a laboratory whose H5N1 test results are accepted by WHO as confirmatory:
  - **Isolation of a HAI A (H5N1) virus**
  - Positive H5 PCR results from tests using two different PCR targets, e.g. primers specific for influenza A and H5 HA
  - A fourfold or greater rise in neutralization antibody titre for H5N1 based on testing of an acute serum specimen and a convalescent serum specimen
  - A micro-neutralization antibody titre for H5N1 of 1:80 or greater in a single serum specimen collected on Day 14 or later after symptom onset and a positive result using a different serological assay

12. Clinical presentation and schematic flow chart for ILI/SARI/ Suspected human case of AI at the sentinel site and its follow-up



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W.H.O. Case Definition Components

- Clinical: Fever, cough, diarrhoea and shortness of breath
- Epidemiological: Related to source of infection, e.g., contact/exposure to source of infection, consumption of infected food, travel to locations where infection exists or handling materials that may be infected.
- Laboratory: Related to information from the laboratory investigations

- WHO case definitions may be sufficient in terms of providing operational case definitions for an outbreak investigation. It should be noted that as more data are made available regarding clinical, laboratory and epidemiological features, the 'status' or 'case definition category' may change with respect to (specific *time, person and place* components). Use of good clinical judgement to the process of modifying such 'set' definitions to the local situation may be generally advised to avoid missing any potential cases.
- In clinical situations requiring decisions on laboratory testing and management of patients with suspected H5N1 infection, any such decisions should be primarily based on clinical judgement and not on strict adherence to the case definitions.

Reporting procedure of Weekly SARI cases and Immediate reporting of PUI / Suspected / Probable case of Human AI

- SARI cases are to be reported weekly to the VBRTDC on EWARS 3 form
- Cases of human AI (PUI / suspected case or probable case of human AI) should be immediately reported to DHO/DPHO/ Regional Directorate / EDCD on EWARS –2 form.
- Health staff should also be vigilant about any report or instance of any unusual death of domestic fowls and or wild birds in the community. In such cases they should contact the local livestock department officials and also inform the same to the DPHO/DHO office.

ANNEX-1

Surveillance Definitions

Active surveillance: Routine surveillance where reports are sought dynamically from participants in the surveillance system on a regular basis (e.g. telephoning each participant monthly to ask about new cases)

Agent: A factor, such as a microorganism, chemical substance, or form of radiation, whose presence, excessive presence, or (in deficiency diseases) relative absences is essential for the occurrence of a disease.

Biologic transmission: The indirect vector-borne transmission of an infectious agent in which the agent undergoes biologic changes within the vector before being transmitted to a new host.

Carrier: A person or animal without apparent disease who harbors a specific infectious agent and is in apparent throughout its course (known as asymptomatic carrier), or during the incubation period, convalescence, and post convalescence of an individual with a clinically recognizable diseases. The carrier state may be of short or long duration (transient carrier or chronic carrier).

Case: In epidemiology, a countable instance in the population or study group of a particular disease, health disorder, or condition under investigation. Sometimes, an individual with the particular disease, or an individual who meets the case definition of the particular disease.

Case definition: A set of diagnostic criteria that must be fulfilled to be regarded as a case of a particular disease or health-related condition. Case definitions can be based on clinical criteria, laboratory criteria or combination of the two.

Case classification: Gradations in the likelihood of being a case (e. g. suspected/probable./confirmed). This particularly useful where early reporting of cases is important (e. g. Ebola haemorrhagic fever) and where there are difficulties in making definite diagnoses (e.g. specialized laboratory tests required).

Case-based surveillance: The surveillance of a disease by collecting specific data on each case (e.g. collecting details on each case of Acute flaccid Paralysis in polio surveillance)

Common source outbreak: An outbreak that results from a group of persons being exposed to a common noxious influence, such as an infectious agent or toxin. If the group is exposed over a relatively brief period of time, so that all cases occur within one incubation period, then the common source outbreak is further classified as a *"point source outbreak"*. In some common source outbreaks, persons may be exposed over a period of days, weeks or longer, with the exposure being either *intermittent or continuos.*

Contact: An individual who has had contact with a source of an infection, a person so exposed or a case, in a way that is considered to have cause significant exposure and therefore risk of infection.

Contagious: capable of being transmitted from one person to another by contact or close proximity.

Direct transmission: the immediate transfer of an agent from a reservoir to a susceptible host by direct contact or droplet spread.

Droplet nuclei: The residue of dried droplets that may remain suspended in the air for long periods, may be blown over great distances, and are easily inhaled into the lungs and exhaled.

Droplet spread: The direct transmission of an infectious agent from a reservoir to a susceptible host by spray with relatively large, short-ranged aerosols produced by sneezing, coughing or talking.

Endemic disease: The constant presence of a disease within a given geographic area or population group.

Epidemic: The occurrence of cases of an illness clearly in excess of expectancy in a given area or among a specific group of people over a particular period of time. This is often referred to as an outbreak (more neutral).

Epidemic period: A time period when the number of cases of disease reported is greater than expected.

Feedback: The regular process of sending analyses and surveillance reports on the surveillance data back through all levels of the surveillance system so that all participants can be informed of trends and performance.

Health event: Any event relating to the health of an individual (e.g the occurrence of a specific disease or syndrome, the administration of a vaccine or an admission to hospital).

Health Information System: A combination of health statistics from various sources, used to derive information about health status, health care, provision and use of services, and impact on health.

Host: A person or other living organism that can be infected by an infectious agent under natural conditions.

Host factor: An intrinsic factor (age, race, behaviors, etc.) which influences and individual's exposure, susceptibility, or response to a causative agent.

Immunity, Active: Resistance developed in response to stimulus by an antigen (infecting agent or vaccine) and usually characterized by the presence of antibody produced by the host.

Immunity, passive: Immunity conferred by an antibody produced in another host and acquired naturally by an infant from its mother, or artificially by administration of an antibody-containing preparation (antiserum or immune globulin).

Incidence: The number of persons who fall ill with a certain disease during a defined time period

Incubation period: a period of sub-clinical or in apparent pathologic changes following exposure, ending with the onset of symptoms of infectious disease.

Indirect transmission: The transmission of an agent carried from a reservoir to a susceptible host by suspended air particles or by animate (vector) or inanimate (vehicle) intermediaries.

Infectious disease: An illness due to a specific infectious agent or its toxic products that arises through transmission of that agent or its products from an infected person, animal, or reservoir to a susceptible host, either directly or indirectly through an intermediate plant or animal host, vector, or inanimate environment.

Laboratory surveillance: surveillance where the starting point is the identification or isolation of a particular organism in a laboratory. (e.g. surveillance of salmonellosis).

Latency period: A period of sub-clinical or innaparent pathological changes following exposure, ending with the onset of symptoms of a chronic disease.

Morbidity: Any departure, subjective or objective, from a state of physiological or psychological well being.

Mortality rate: A measure of frequency of occurrence of death in a defined population during a specified interval of time.

Notificable disease: A disease that must be reported to the authorities by law or ministerial decree.

Outbreak: The occurrence of two or more linked cases of a communicable disease. Synonymous with epidemic. Sometimes the preferred word, as it may escape sensationalism associated with the word epidemic. Alternatively, a localized as opposed to generalized epidemic.

Pandemic: an epidemic occurring over a very wide area (several countries or continents) and usually affecting a large proportion of the population.

Passive surveillance: Routine surveillance where reports are awaited and no attempt make actively seek reports from the participants in the system.

Pathogenicity: The proportion of persons infected, after exposure to a causative agent, who then develop clinical disease.

Reporting completeness: Proportion of all expected reports that were actually received (usually state as "% completeness as of a certain date").

Reporting timeliness: Proportion of all expected reports that were received by a certain due date.

Reporting system: The specific process by which diseases or health events are reported. This will depend on the importance of the disease and the type of surveillance.

Reservoir: The habitat in which an infectious agent normally lives, grows and multiplies; reservoirs include human reservoirs, animal reservoirs and environmental reservoirs.

Risk: The probability that an event will occur, e.g. that an individual will become ill or die within a stated period of time or age.

Risk factor: an aspect of personal behavior or lifestyle, an environmental exposure, or an inborn or inherited characteristic that is associated with an increased occurrence of disease or other health-related event or condition.

Routine surveillance: the regular systematic collection of specified data in order to monitor a disease or health event.

Sentinel surveillance: A surveillance system in which a per-arranged sample of reporting sources, agrees to report all cases of one or more notifiable conditions. The sample should be representative of the total population at risk.

Surveillance: The systematic collection, analysis, interpretation and dissemination of health data on an ongoing basis to those who need to know, to gain knowledge of the pattern of disease occurrence and potential in a community, in order that action may be taken to control and prevent disease in that community.

Transmission of infection: Any mode or mechanism by which an infectious agent is spread through the environment or to another person.

Vector: An animate intermediary in the indirect transmission of an agent that carries the agent from a reservoir to a susceptible host.

Vehicle: An inanimate intermediary in the indirect transmission of an agent that carries the agent from a reservoir to a susceptible host.

Zero reporting: The reporting of zero cases when no case have been detected by the participant. This allows the next level of the system to be sure that the participant has not sent data has been lost or has forgotten to report.

Zoonoses: An infectious disease that is transmissible under normal conditions from animals to humans.

ANNEX- 2

COLLECTION, STORAGE AND TRANSPORT OF HUMAN SPECIMENS

1. Collection of Human Specimens

1.1 For serological diagnosis

Venous blood specimens should be collected from suspected JE cases as early as possible in the acute phase, immediately after admission to the hospital or attendance at the clinic. A second, convalescent specimen should be collected later on, at the time of discharge from the hospital, if that comes first.

Five ml of blood is collected aseptically. The blood should be kept at room temperature for about 15 minutes to enable it to clot. Then at 4^0 C the clot is allowed to retract. The serum is separated from the clot and is transferred to a tightly stopped sterile container.

The container is sealed with adhesive tape; adhesive tape should also be used for a late, and the patient's name, identification number and date should be written clearly in pencil or indelible ink or typewritten.

Place serum if a refrigerator for storage prior to transportation to the laboratory.

Alternatively blood can be collected in capillary tubes or on filter paper strips properly labeled. The blood soaked filter paper strips need to be dried in air, before they are sealed in an envelope. CSF specimens should be collected aseptically and placed in labeled containers.

1.2 For Virus Isolation

CSF specimens collected during the early acute phase labeled and inoculated into cells, such as AP61 cells at the bedside. It bedside inoculation is not possible; the specimen must be frozen on dry ice and transported to a laboratory immediately.

Brain tissue obtained from patients dying during the first two weeks of illness is the best source for the isolation of virus. Small pieces of brain tissue collected at autopsy should be obtained from different parts of the brain- cerebral cortex, cerebellum, basal nuclei and brain stem. If a full post mortem is not possible, small pieces of cerebral tissue may be obtained with the aid of a trephine. If even this procedure is not permitted, small pieces of brain tissue can be obtained by biopsy, using a Vim-Silverman needle inserted via the nose through the cribiform plate of the ethmoid bone.

The brain tissue(s) thus obtained should be immersed in 2 ml of transport medium available, 10% glycerol saline (pH 7.4) may be used. Alternatively, nutrient broth

medium with antibiotics can be used. The container used should be moderately thick glass and should preferably be screw capped.

2. Storage and transport

Specimen should be placed in a refrigerator at 4^0C as soon as possible after collection. Do not freeze the specimens. They should be dispatched at the earliest possible opportunity in a large thermos or in an icebox to the central or referral laboratory on wet ice. They can either be air freighted or sent by road through as special courier. The courier should drain the water and replenish ice as and when required during the journey.

Specimen for virus isolation attempts should ideally be transported in sealed containers in dry ice or liquid nitrogen. In most places, however, such facilities are not available.