HAND FOOT AND MOUTH DISEASE (HFMD) GUIDELINES

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1. INTRODUCTION

Hand foot and mouth disease (HFMD) is typically a benign and common illness among children and infants characterized by rapidly ulcerating vesicles in the mouth and lesions, usually vesicular, on the hands and feet.[1] HFMD is an endemic disease in Malaysia. HFMD has become an important public health disease due to its tendency to cause large outbreaks and deaths among children and infants. The purpose of the guidelines is to help health personnels and health authorities, at any levels;

- To update current knowledge about HFMD
- To detect and control epidemic of HFMD as early as possible
- To strengthen the capacity for emergency response to epidemics of HFMD
- To improve the outcome of HFMD cases through effective case management.

2. THE DISEASE

Hand foot and mouth disease (HFMD) is caused by systemic infections with human enteroviruses. Human enteroviruses comprise one genus in the family Picornaviridae, which also contains the genera rhinovirus, cardiovirus, aphthovirus, hepatovirus and parechovirus. The members of the enterovirus genus that infect humans include the polioviruses, the Coxsackie virus groups A and B, the echoviruses and the enteroviruses 68-71.[2]

2.1 Transmission

Hand foot and mouth disease (HFMD) is moderately contagious. Infection is spread from person to person by direct contact with nose and throat discharges, saliva, fluid from blisters, or the stool of infected persons. A person is most contagious during the first week of the illness.

2.2 Clinical Features

HFMD is characterised by vesicular eruptions on the hands, wrists, feet and within the mouth. Lesions on the hands are almost always present, but oral lesions are present in 90% of patients and can occasionally be the only manifestation of the disease. The oral vesicles are often on the palate, tongue, and buccal mucosa and may range from a few isolated lesions to a marked stomatitis.

In addition patients may suffer fever, malaise, conjunctival injection, headache, and abdominal pain and occasionally diarrhea. The lesions on the feet and hands are flaccid, grayish vesicles, most often on the sides of the fingers, instep and

toes. If the disease is confined to the oral cavity it is almost indistinguishable from primary herpetic gingivostomatitis.[3]

Hand foot and mouth disease may be related to coxsackieviruses A16, A5, A9, A10, B2, B5 and enterovirus 71. Coxsackievirus A16 (Cox A16) is a frequently encountered pathogen in cases of HFMD and its clinical course is usually uneventful, with full recovery.

Fatal cases of Cox A16 infection are rare. Literature search revealed only three fatal cases of Cox A16 since 1963. All the cases were infants. The first case was reported by Wright et al in 1963 involving a 10 month-old girl with respiratory infection.[4] The second case involved a 7 month-old boy with grunting and tongue ulcers.[5] The third case was reported by Wang et al involving a 15 month-old boy who presented with hand foot and mouth disease complicated with myocarditis and intractable shock.[6]

HFMD caused by enterovirus 71 (EV71) can be more severe and may be complicated with meningitis, encephalitis and neurogenic pulmonary edema. In Taiwan, based on 1998 epidemic, the significant difference in the clinical features of Coxsackievirus A16 infection and EV 71 infection was that in EV71 the fever was usually higher than 39°C and longer than 3 days.[7]

Enterovirus 71 infection can be classified into 4 stages:

Stage 1 – Hand foot and mouth disease (HFMD), oral ulcers and vesicular rash appearing on the hands, feet, knees and / or buttocks; or herpangina including oral ulceration over anterior tonsillar pillars, the soft palate, buccal mucosa or uvula.

Stage 2 – CNS involvement - aseptic meningitis with headache, irritability or myoclonic jerk and CSF pleocytosis (> 5 x 10^6 leucocytes / litre) but without altered level of consciousness and focal signs, or encephalitis with altered level of consciousness plus CSF pleocytosis or poliomyelitis like syndrome with acute limb weakness and decreased reflex and muscle strength, or encephalomyelitis with the occurrence of both encephalitis and poliomyelitis like syndrome.

Stage 3 – Cardiopulmonary failure, pulmonary edema or hemorrhage with decreased ejection fraction of left ventricle as assessed by echocardiography necessitating inotropic agent support.

Stage 4 – Convalescence - is defined as recovery from cardiopulmonary failure.

2.3 Magnitude of the disease

Hand foot and mouth disease (HFMD) generally is a common and self limiting disease among children. EV 71 infection is the more important public health concern. In temperate countries most HFMD cases occur in the summer and fall and the incubation period is 4 – 6 days.

EV 71 was first isolated from a child with aseptic meningitis in California in 1969, and by 1974, the virus had been described as a new serotype of genus *Enterovirus.* In the years following the initial isolation of EV71, outbreaks occurred in USA, Australia, Sweden and Japan. In 1975 EV71 gained global attention when it was responsible for an outbreak in Bulgaria that resulted in 705 cases of poliomyelitis-like disease and the deaths of 44 people; 93% of the poliomyelitis-like disease cases occurred in children under the age of five. A similar outbreak occurred in Hungary in 1978, which also involved many cases of poliomyelitis-like disease and 47 deaths. Since this time outbreaks of EV71 have continued to occur throughout the world.

More recently there has been an increase in EV71 activity in the Asia Pacific region with several epidemics of HFMD being reported, including multiple cases associated with brain stem encephalitis and pulmonary edema. The first such epidemic occurred in Sarawak (Malaysian Borneo) in 1997 followed by smaller outbreaks in peninsular Malaysia and Japan. In 1998 outbreaks continued in Singapore and Taiwan.

The outbreak that occurred in Taiwan is the largest recorded, with greater than 100,000 cases of HFMD. Of these 400 children were admitted to hospital with central nervous system (CNS) involvement and 78 died of brainstem encephalitis with neurogenic pulmonary oedema.[8] In 1999, a large HFMD outbreak occurred in Perth, western Australia and in 2000, EV71 was the cause of epidemics in Korea, Japan, Singapore, Taiwan and peninsular Malaysia, resulting in a range of clinical presentations including HFMD, aseptic meningitis, encephalitis and poliomyelitis like disease. Another outbreak occurred in Sarawak in 2003 which coincide with the SARS outbreak in the region and the public health measures put into place during this time evidently served to control transmission of enteroviruses as well.[9]

3. CLINICAL MANAGEMENT OF HFMD

HFMD is usually a mild and self limiting. In general, most cases of HFMD do not require admission but can be managed as outpatients. Most fatal HFMD cases were due to enterovirus infection.

3.1 Symptomatic treatment

Mild HFMD cases only need symptomatic treatment. Treatment of fever and relief of symptoms, adequate hydration and rest are important. Parents and care takers should be educated on hygiene and measures that they should take to prevent transmission to other children.

3.2 Hospitalisation.

3.2.1 Criteria for admission

- When the child is unable to tolerate oral feeds and there is a need for intravenous hydration;
- When the child is clinically very ill or toxic-looking
- When some other more serious disease cannot be excluded
- When there is persistent hyperpyrexia (e.g >38ºC) for >48 hours;
- When there is a suspicion of neurological complications, e.g increased lethargy, myoclonus, increased drowsiness, change in sensorium and/or seizures;
- When there is a suspicion of cardiac complications (myocarditis), e.g low blood pressure, low pulse volume, heart rhythm abnormalities, murmurs, gallop rhythm, displaced apex beat;
- When parents are unable to cope with child's illness; and
- When there is inadequate family or social support in looking after the child at home.

3.2.2 Infection control

- Proper hygiene including mandatory hand washing after contact with patient, appropriate cleanliness during diaper changes is imperative
- Personal items such as spoons, cups and utensils should not be shared and should be properly washed with detergent after use;
- The use of gowns may act as a useful protection for health personnel looking after these patients; and
- Patients with HFMD should be isolated and the usual isolation procedures followed for infection control.

3.3 Patients with neurologic complication

Huang et al reviewed HFMD cases in Taiwan in 1998 and they found that the mean age of patients with neurological manifestations was 2.5 (range, 3 months to 8.2 years[10]. Higher incidence occurs in the younger age group. The neurologic disorders usually began 2 to 5 days after the onset of skin or mucosa lesion or fever.

Wu JM et al carried out a prospective study among infants confirmed to have enterovirus 71 and found that[11];

- EV71 infection can lead to severe neurologic complications and acute pulmonary edema with or without hemorrhage
- All patients with EV71 infection and pulmonary edema had brainstem lesions
- Viral myocarditis is not the direct cause of acute PE and cardiopulmonary failure in EV71 Infection
- The excessive central sympathetic activation resulting in vasoconstriction was not the major cause of PE or hemorrhage

Based on the findings, they suggested that;

- Vasodilators should be used with caution since pulmonary edema in EV71 infection is not resulting from excessive vasoconstriction alone
- Cardiopulmonary function usually returns to nearly normal within days but the neurogic sequelae are severe and usually permanent. Therefore the use of extracorporeal membrane oxygenation support or a heart assist device should be weighed carefully
- Direct intracardiac hemodynamic monitoring may provide additional information to guide critical care

3.4. ADVICE GIVEN UPON PATIENT'S DISCHARGE

Parents and guardians should be advised upon patients discharge on complications that may occur; a statement as shown below can be given:

> "Your child has been diagnosed to have hand-foot-mouth disease. This disease is normally not dangerous but in the light of recent events, we advise that you bring back your child to this hospital if he / she has any of the following symptoms:
>
> - High fever.
> - Lethargy and weakness.
> - Refusing feeds and passing less urine.
> - Rapid breathing.
> - Vomiting.
> - Drowsiness or irritably.
> - Fits."

4. SURVEILLANCE

The actual burden of HFMD in this country is not known. HFMD surveillance in Malaysia started after the Sarawak outbreak in 1997 with sentinel surveillance. Both private and government clinics were included as sentinel sites for each district. The number of sentinel sites for each district depends on the assumed prevalence of HFMD in the district / state.

HFMD notification is administratively required and started since October 2005. However death of HFMD and admitted cases to the ward of children aged 10 years old and below is mandatory for notification. However due to frequent outbreaks and fatality in Sarawak, Sarawak State has required all HFMD cases in the state to be notified.

The notification of HFMD came into enforcement on 12 October 2006 under the PU.A 374 / 2006 (appendix 1).

3.1 Objective of surveillance

i. To detect impending outbreak.
ii. To monitor circulating infectious agent.
iii. To estimate the magnitude of HFMD in the population at risk.
iv. To estimate the magnitude of the HFMD complication in the population at risk.

3.2 Case definition

3.2.1 Clinical case definition

3.2.1.1 Case of HFMD:

Any child with:

a. mouth / tongue ulcer **and**
b. maculopapular rashes and / **or** vesicles on palms and soles
c. **with OR without** history of fever

3.2.1.2 HFMD myocarditis:

2(i) **Suspected HFMD myocarditis**

Asymptomatic child with unexplained tachycardia to fulminant congestive cardiac failure.

With history of dirrhoea or URTI.

Accompanied by fever, malaise, tachypnoea, tachycardia (above and beyond expected for age and fever) or dehydration.

Pallor and shock in the absence of or obvious pulmonary sign or in the presence of crepitations (no murmurs) and / or a clinically enlarged heart.

2(i) **Confirmed HFMD myocarditis**.

The above 2(i) with virologic confirmation of enteroviruses.

3.2.1.3 HFMD meningoencephalitis / AFP

3(i) **Suspected HFMD meningoencephalitis**

Evidence of aseptic meningitis.

Evidence of aseptic encephalitis.

Evidence of AFP.

3(ii) **Confirmed HFMD meningoencephalitis / AFP.**

The above 3(i) with virologic confirmation of enteroviruses

3.2.2 Laboratory criteria

Any case that has the clinical symptoms and positive for viruses (coxsackieviruses (Cox) A16, A5, A9, A10, B2, B5 and enterovirus (EV) 71) which could cause HFMD, isolated or detected from stool or vesicle fluid or mouth ulcer or saliva.

3.2.3 Case classification

Suspected: A case that meets the clinical case definition.

Confirmed: A suspected case in which laboratory investigation confirms the presence of virus OR when cases are epidemiologically linked to a laboratory confirmed case.

3.3 Types of surveillance

3.3.1 Clinical surveillance

It is mandatory to notify HFMD under the National Notification of Infectious Diseases (list of notifiable diseases). Notification must be done within 24 hours of diagnosis via telephone, then it should be followed by notification form.

All HFMD cases detected must be entered to CDCIS. If states have other methods of data storing, it must be shared with MOH.

Laboratory confirmation is **NOT** required for notification.

3.2.2 Laboratory surveillance

Sentinel sites

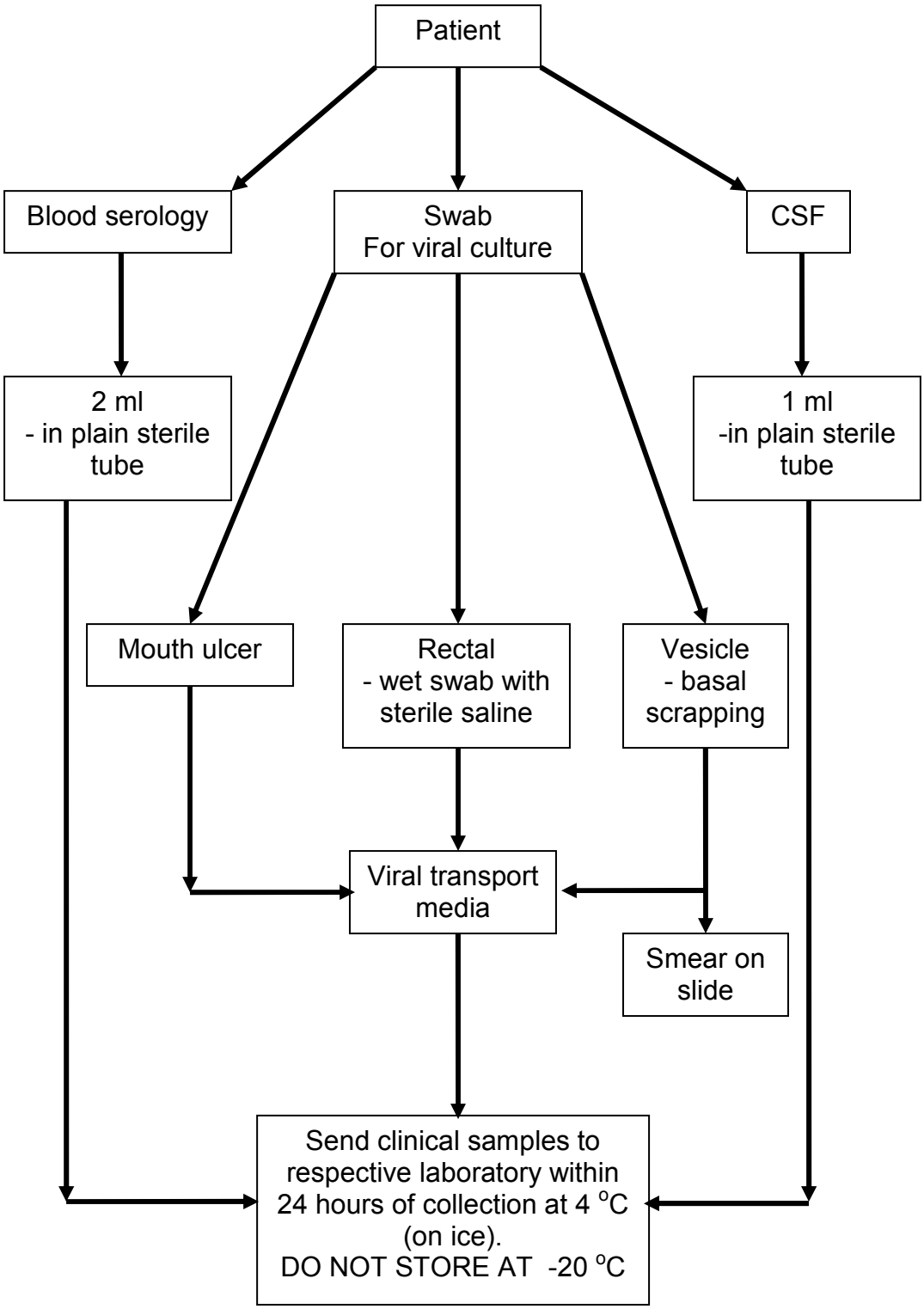
Enterovirus surveillance is done through state's sentinel sites. A state has to choose two sentinel sites. Preferably the sites have a considerable numbers of children cases as HFMD prevalence is higher among this age group. At least 5 specimens from 5 patients per centre should be taken and sent to the designated laboratory (as in table below). Please use the laboratory request form as in appendix 2(i).

Designated laboratory involves in enterovirus surveillance

Laboratory	Contact number	Respective states
IMR	03-26988792	Johor, WPKL, Melaka, Pahang.
UMMC	03-79675756 / 79676678	Selangor.
NPHL	03-61402213	Perlis, Kedah, Perak, Penang
HUKM	03 - 91702203 / 2208	Negeri Sembilan
USM	09 - 7664602 / 4609 / 3000 ext 4602	Terengganu, Kelantan

Surveillance for Sarawak and Sabah is expected to start once Kota Kinabalu Public Health Laboratory is ready to function.

Clinical Specimen Collection, Handling And Transportation

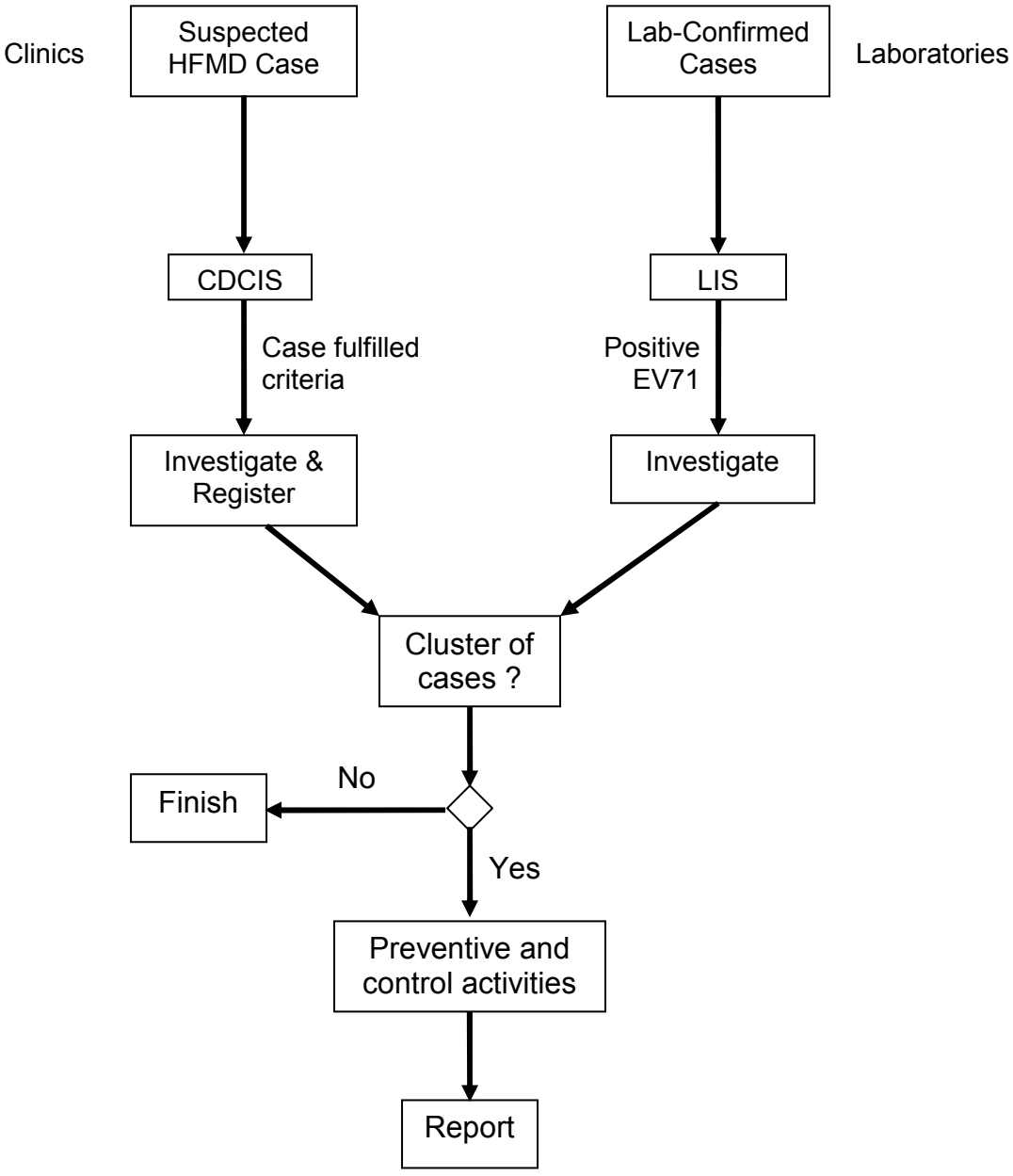


3.4 Flow of surveillance data

Notification data should be entered in CDCIS as and when there is HFMD case. Other sources of data must be shared with Disease Control Division. Data must have the variables listed in appendix 1.

Laboratory results for enterovirus surveillance must be shared with respective states and Disease Control Division using the suggested format in appendix 2(ii).

Flow of Information Management



5. MANAGEMENT OF SPORADIC CASES

5.1 Definitions of sporadic case:

A single case of HFMD in the absence of previous known close contact with another case.

5.2 The public health measures

5.2.1 Case Investigation

Case investigation is required following the criteria below:

a. every notified HFMD case that fulfilled any one of the criteria below:

   i. case is admitted to hospital
   ii. case died.
   iii. case aged 6 years and below **and** goes to any pre-schools or nurseries.

The first two criteria indicate severity of illness and it is a proxy of possible EV71 infection. Meanwhile the third criterion is important in preventing spread of illness among the pre-school children (high risk group) and reducing public anxiety.

b. every case with positive EV71 laboratory result.

Investigation should be carried out to determine the course, source and severity of infection. Enquiries shall be made into;

1. Particulars of the person affected
2. Clinical signs and symptoms with date of onset. In addition, enquiries shall be elicited for associated complications e.g. seizures, weakness of limbs, staring episodes, drowsiness, profound lethargy and refusal to play.

   Enterovirus infections that are not associated with complications may not have cutaneous manifestations.
3. Duration of illness
4. Type of treatment sought, including details of hospitalization and reason for admission
5. History of travel especially to outbreak area in the past two weeks
6. Contacts with similar illness in an institution (child care centre or kindergarten), family or neighbourhood where relevant.
7. If newborn, antenatal history including maternal history of febrile illness, mode of delivery

5.2.2 Incidence management

Following steps should be taken to prevent further spread of disease / pathogen:

1. Ensure that the infected children remain away from the institution for at least ten days after onset of symptoms and must be certified free from infection by a registered medical practitioner prior to returning to school.
2. Active case detection shall be carried out among contacts in the institution and family, and all those with illness shall be referred for treatment at the nearest health clinics.
3. Swabs from oral ulcers and vesicular lesions on the hands and feet shall be collected for virus isolation at identified laboratories (IMR or NPHL). If these ulcers and vesicles are no longer present, stool specimens shall be sent. Always consult pathologist for specimens taking, handling and transportation.
4. Health education of supervisors of institutions on the disease, mode of transmission, importance of good personal hygiene and isolation of infected children shall be carried out.
5. Principals, teachers and supervisors shall be alerted to look out for children with fever, rash / blisters on palms and soles and to isolate them immediately. Screening before coming to class is recommended (please refer *Buku Panduan Latihan Taska dan Prasekolah*).
6. If there are two or case in the premise, advice the premise to be closed to cut disease transmission. It should be closed for two incubation period (10 days) from the date of onset of the last case.
7. Supervision on disinfection procedures shall be given to the premise operators. Articles such as toys contaminated by infected cases are disinfected with 0.5% sodium hypochlorite solutions (please refer *Buku Panduan Latihan Taska dan Prasekolah*).

6. MANAGEMENT OF OUTBREAK

6.1 Definitions of outbreak

The occurrence of two or more cases in the same locality within the incubation period.

Organisation based outbreak – two or more cases with onset in two weeks interval in a group which makes epidemiological sense.

6.2 Identification of outbreaks

Surveillance data on HFMD cases should be reviewed on continuous basis to identify cases and detects outbreaks.

6.3 Risk factors for outbreaks

Risk factors for outbreaks are not completely understood. A combination of conditions (environment, host and organism) is necessary for an epidemic to occur. However large HFMD outbreaks have been associated with EV71 infection.

6.4 Management of outbreaks

When a suspected outbreak is reported, it is important to determine rapidly whether a true outbreak is occurring based on the definition above.

Similar steps as in sporadic case management should be carried out together with following measures;

1. Ensure that the infected children remain away from the institution for at least ten days after onset of symptoms and must be certified free from infection by a registered medical practitioner prior to returning to school.
2. An assessment of the number of cases and susceptible population involved shall be made, and the overall attack rate and age-specific attack rate computed.
3. Active case detection shall be carried out among contacts in the institution and family, and all those with illness shall be referred for treatment at the nearest health clinics.
4. Where a case is observed or suspected to have unusual signs and symptoms e.g. seizures, weakness of limbs, profound lethargy, refusal to play, the case shall be immediately referred to hospital.
5. Swabs from oral ulcers and vesicular lesions on the hands and feet shall be collected for virus isolation at identified laboratories (IMR or NPHL). If these ulcers and vesicles are no longer present, stool specimens shall be sent. Always consult pathologist for specimens taking, handling and transportation.

6. Principals, teachers and supervisors shall be alerted to look out for children with fever, rash / blisters on palms and soles and to isolate them immediately. Screening before coming to class is recommended (please refer *Buku Panduan Latihan Taska dan Prasekolah*).
7. Health education of supervisors of institutions on the disease, mode of transmission, importance of good personal hygiene and isolation of infected children shall be carried out.
8. Close the premise closed for two incubation period (10 days) from the date of onset of the last case. Supervision on disinfection procedures shall be given to the premise operators.

In addition the investigating team shall also look into environmental sanitation and hygiene to ensure that:

a. Articles such as toys contaminated by infected cases are disinfected with 0.5% sodium hypochlorite solutions (please refer *Buku Panduan Latihan Taska dan Prasekolah*).
b. A high standard of food and personal hygiene is maintained by the institution involved which include proper waste and diapers disposal.
c. The approved enrolment of Department of Social Welfare (JKM), Ministry of Education, Department of National Integration and other relevant parties, where applicable, and shall notify the relevant authorities if regulations not complied.

If the outbreak occurs in primary schools;

i. Ensure that the infected students remain away from the institution for at least ten days.
ii. Health education to the students on the disease, mode of transmission, importance of good personal hygiene.
iii. Principals, teachers and supervisors shall be look for children with fever, rash / blisters on palms and soles and to isolate them immediately. Screening before coming to class is recommended (please refer *Buku Panduan Latihan Taska dan Prasekolah*).
iv. If closure is necessary, just closed the affected class. Closure of the whole school is unnecessary as HFMD in older children is usually very mild and so far no complication has been documented from this agegroup.

6.5 Documentation and review

Disease activity and emergency response should be adequately documented so that further outbreaks can be handled more effectively. A summary report should be prepared within a month from the last date of case; and distributed to all the stakeholders for feedback. Format of report, dissemination and tabling of report is discussed in more details in Infectious Disease Outbreak Rapid Response Manual.[12]

Appendix 1

Variables required in HFMD surveillance database

1 Epid week
2 Name
3 Age
4 Sex
5 Ethnic
6 Home address
7 Locality
8 District
9 Name of school / preschool / nursery
10 Address of school / preschool / nursery
11 Date of onset
12 Case definition fulfilled
13 Symptoms and signs of CNS
14 Contact with HFMD case
15 Address of contact
16 Date of seen
17 Name of clinic / hospital
18 Government or private health facility
19 Outpatient or inpatient treatment
20 Date of admitted
21 Date of discharge
22 Date of death

Appendix 2(i)

No. Rujukan Makmal	

NATIONAL ENTEROVIRUS SURVEILLANCE
DIAGNOSTIC REQUEST FORM

A. MAKLUMAT PESAKIT		
Negeri :	Daerah :	
Hospital (wad) / Klinik Kesihatan		No. R/N :
Nama Pesakit :		
No. K/P :	Umur :	Jantina : L / P
Bangsa :	Tarikh lahir :	

B. MAKLUMAT KLINIKAL		
Gejala (Simptom)	Ada / Tiada (Tandakan √)	Tarikh mula
Demam > 38 ^{0}C		
Ulser di mulut & tekak		
Maculopapular rashes dan / Vesikel pada tapak tangan dan tapak kaki		
Tanda dan gejala URTI		

C. SPESIMEN KLINIKAL			
Spesimen		**Tarikh diambil**	**Tarikh penghantaran**
Rectal swab		/ /	/ /
Mouth ulcer		/ /	/ /
Vesicle swab		/ /	/ /
Stool		/ /	/ /

D. MAKLUMAT PEMOHON	
Nama dan Cop Pegawai : Tandatangan :	No. telefon : No. fax : e-mail :

E. MAKMAL (Untuk Kegunaan Makmal)			
Keadaan spesimen :			Tarikh terima spesimen :
Spesimen	**Jenis ujian**	**Keputusan ujian**	**Komen**
Rectal swab			
Mouth ulcer			
Vesicle swab			
Stool			

Nama dan tandatangan Pegawai Makmal :	
Jawatan Pegawai Makmal dan Cop Makmal :	Tarikh :

Nota * : All samples except blood / serum and stool must be in the viral transport media (VTM) and send immediately in ice pack to HUKM Microbiological Laboratory.

Appendix 2(ii)

Variables Required for Enterovirus Surveillance Database

Name of Centre / Laboratory: _____

No	Date Sample Received	Date Sample Collected	LN	RN	Name	Ethnic	Age	Sex	Source	Case diagnosis	Type of spec	Result		
												IF	Isolation	PCR

BORANG SIASATAN PESAKIT DI WAD
PENYAKIT TANGAN, KAKI DAN MULUT (HFMD)
BAHAGIAN KAWALAN PENYAKIT, KEMENTERIAN KESIHATAN MALAYSIA

BAHAGIAN 1

Tarikh masuk wad: ☐☐☐☐☐☐ Masa: ☐☐☐☐

Tarikh discaj: ☐☐☐☐☐☐ Masa: ☐☐☐☐

Tarikh kematian ☐☐☐☐☐☐ Masa: ☐☐☐☐

A. PERIHAL PESAKIT

1. Nama pesakit:
2. Tarikh lahir: ☐☐☐☐☐☐
3. Nama ibu:
4. No K/P ibu:
5. Alamat rumah:
6. No telefon: (rumah)
(H/P)

Kedudukan rumah (GPS): X : _____ Y : _____

7. Jantina: ☐ Lelaki ☐ Perempuan

8. Kumpulan etnik
☐ Melayu ☐ Kadazan/Dusun
☐ Cina ☐ Murut
☐ India ☐ Bajau
☐ Asli semenanjung ☐ Melanau
☐ Bidayuh ☐ Iban
☐ Lain-lain pribumi ☐ Lain-lain (nyatakan)
Sabah/ Sarawak

9. Kewarganegaraan: ☐ Malaysia ☐ Warga asing

10. Menghadiri sekolah / taska
☐ Ya
☐ Taska / Nurseri
☐ Prasekolah
☐ Sekolah
Nyatakan nama: _____
☐ Tidak

B. MAKLUMAT KLINIKAL

1. Tarikh mula sakit (onset) ☐☐☐☐☐☐☐☐

2. Tanda dan gejala: Ya ☐ Tidak ☐
Riwayat demam

Ulser mulut	☐	☐
Ruam (rash) tapak tangan / kaki	☐	☐
vesicles di tapak tangan / kaki	☐	☐

3. Kompliksi	Ya	Tidak
Aseptic meningitis	☐	☐
Myocarditis	☐	☐
Encephalitis	☐	☐
Acute flaccid paralysis	☐	☐
Jika ya, sila nyatakan bahagian anggota: _____		
Kematian	☐	☐

C. MAKLUMAT UJIAN MAKMAL

SAMPEL	Tarikh diambil	Keputusan	Tarikh keputusan
Throat swab			
Rectal swab			
Vesicle swab			
Stool			
Blood			
CSF			
Biopsy _____ (Nyatakan tisu)			

D. MAKLUMAT PEGAWAI YANG MERAWAT

1. Nama Pakar / Pegawai Perubatan: _____ Tandatangan: _____
2. Nama Wad: _____
3. Nama hospital: _____ Tarikh notifikasi: _____

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HAND FOOT AND MOUTH DISEASE (HFMD) GUIDELINES

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1. INTRODUCTION

Hand foot and mouth disease (HFMD) is typically a benign and common illness among children and infants characterized by rapidly ulcerating vesicles in the mouth and lesions, usually vesicular, on the hands and feet.[1] HFMD is an endemic disease in Malaysia. HFMD has become an important public health disease due to its tendency to cause large outbreaks and deaths among children and infants. The purpose of the guidelines is to help health personnels and health authorities, at any levels;

- To update current knowledge about HFMD
- To detect and control epidemic of HFMD as early as possible
- To strengthen the capacity for emergency response to epidemics of HFMD
- To improve the outcome of HFMD cases through effective case management.

2. THE DISEASE

Hand foot and mouth disease (HFMD) is caused by systemic infections with human enteroviruses. Human enteroviruses comprise one genus in the family Picornaviridae, which also contains the genera rhinovirus, cardiovirus, aphthovirus, hepatovirus and parechovirus. The members of the enterovirus genus that infect humans include the polioviruses, the Coxsackie virus groups A and B, the echoviruses and the enteroviruses 68-71.[2]

2.1 Transmission

Hand foot and mouth disease (HFMD) is moderately contagious. Infection is spread from person to person by direct contact with nose and throat discharges, saliva, fluid from blisters, or the stool of infected persons. A person is most contagious during the first week of the illness.

2.2 Clinical Features

HFMD is characterised by vesicular eruptions on the hands, wrists, feet and within the mouth. Lesions on the hands are almost always present, but oral lesions are present in 90% of patients and can occasionally be the only manifestation of the disease. The oral vesicles are often on the palate, tongue, and buccal mucosa and may range from a few isolated lesions to a marked stomatitis.

In addition patients may suffer fever, malaise, conjunctival injection, headache, and abdominal pain and occasionally diarrhea. The lesions on the feet and hands are flaccid, grayish vesicles, most often on the sides of the fingers, instep and

toes. If the disease is confined to the oral cavity it is almost indistinguishable from primary herpetic gingivostomatitis.[3]

Hand foot and mouth disease may be related to coxsackieviruses A16, A5, A9, A10, B2, B5 and enterovirus 71. Coxsackievirus A16 (Cox A16) is a frequently encountered pathogen in cases of HFMD and its clinical course is usually uneventful, with full recovery.

Fatal cases of Cox A16 infection are rare. Literature search revealed only three fatal cases of Cox A16 since 1963. All the cases were infants. The first case was reported by Wright et al in 1963 involving a 10 month-old girl with respiratory infection.[4] The second case involved a 7 month-old boy with grunting and tongue ulcers.[5] The third case was reported by Wang et al involving a 15 month-old boy who presented with hand foot and mouth disease complicated with myocarditis and intractable shock.[6]

HFMD caused by enterovirus 71 (EV71) can be more severe and may be complicated with meningitis, encephalitis and neurogenic pulmonary edema. In Taiwan, based on 1998 epidemic, the significant difference in the clinical features of Coxsackievirus A16 infection and EV 71 infection was that in EV71 the fever was usually higher than 39°C and longer than 3 days.[7]

Enterovirus 71 infection can be classified into 4 stages:

Stage 1 – Hand foot and mouth disease (HFMD), oral ulcers and vesicular rash appearing on the hands, feet, knees and / or buttocks; or herpangina including oral ulceration over anterior tonsillar pillars, the soft palate, buccal mucosa or uvula.

Stage 2 – CNS involvement - aseptic meningitis with headache, irritability or myoclonic jerk and CSF pleocytosis (> 5 x 10^6 leucocytes / litre) but without altered level of consciousness and focal signs, or encephalitis with altered level of consciousness plus CSF pleocytosis or poliomyelitis like syndrome with acute limb weakness and decreased reflex and muscle strength, or encephalomyelitis with the occurrence of both encephalitis and poliomyelitis like syndrome.

Stage 3 – Cardiopulmonary failure, pulmonary edema or hemorrhage with decreased ejection fraction of left ventricle as assessed by echocardiography necessitating inotropic agent support.

Stage 4 – Convalescence - is defined as recovery from cardiopulmonary failure.

2.3 Magnitude of the disease

Hand foot and mouth disease (HFMD) generally is a common and self limiting disease among children. EV 71 infection is the more important public health concern. In temperate countries most HFMD cases occur in the summer and fall and the incubation period is 4 – 6 days.

EV 71 was first isolated from a child with aseptic meningitis in California in 1969, and by 1974, the virus had been described as a new serotype of genus *Enterovirus.* In the years following the initial isolation of EV71, outbreaks occurred in USA, Australia, Sweden and Japan. In 1975 EV71 gained global attention when it was responsible for an outbreak in Bulgaria that resulted in 705 cases of poliomyelitis-like disease and the deaths of 44 people; 93% of the poliomyelitis-like disease cases occurred in children under the age of five. A similar outbreak occurred in Hungary in 1978, which also involved many cases of poliomyelitis-like disease and 47 deaths. Since this time outbreaks of EV71 have continued to occur throughout the world.

More recently there has been an increase in EV71 activity in the Asia Pacific region with several epidemics of HFMD being reported, including multiple cases associated with brain stem encephalitis and pulmonary edema. The first such epidemic occurred in Sarawak (Malaysian Borneo) in 1997 followed by smaller outbreaks in peninsular Malaysia and Japan. In 1998 outbreaks continued in Singapore and Taiwan.

The outbreak that occurred in Taiwan is the largest recorded, with greater than 100,000 cases of HFMD. Of these 400 children were admitted to hospital with central nervous system (CNS) involvement and 78 died of brainstem encephalitis with neurogenic pulmonary oedema.[8] In 1999, a large HFMD outbreak occurred in Perth, western Australia and in 2000, EV71 was the cause of epidemics in Korea, Japan, Singapore, Taiwan and peninsular Malaysia, resulting in a range of clinical presentations including HFMD, aseptic meningitis, encephalitis and poliomyelitis like disease. Another outbreak occurred in Sarawak in 2003 which coincide with the SARS outbreak in the region and the public health measures put into place during this time evidently served to control transmission of enteroviruses as well.[9]

3. CLINICAL MANAGEMENT OF HFMD

HFMD is usually a mild and self limiting. In general, most cases of HFMD do not require admission but can be managed as outpatients. Most fatal HFMD cases were due to enterovirus infection.

3.1 Symptomatic treatment

Mild HFMD cases only need symptomatic treatment. Treatment of fever and relief of symptoms, adequate hydration and rest are important. Parents and care takers should be educated on hygiene and measures that they should take to prevent transmission to other children.

3.2 Hospitalisation.

3.2.1 Criteria for admission

- When the child is unable to tolerate oral feeds and there is a need for intravenous hydration;
- When the child is clinically very ill or toxic-looking
- When some other more serious disease cannot be excluded
- When there is persistent hyperpyrexia (e.g >38ºC) for >48 hours;
- When there is a suspicion of neurological complications, e.g increased lethargy, myoclonus, increased drowsiness, change in sensorium and/or seizures;
- When there is a suspicion of cardiac complications (myocarditis), e.g low blood pressure, low pulse volume, heart rhythm abnormalities, murmurs, gallop rhythm, displaced apex beat;
- When parents are unable to cope with child's illness; and
- When there is inadequate family or social support in looking after the child at home.

3.2.2 Infection control

- Proper hygiene including mandatory hand washing after contact with patient, appropriate cleanliness during diaper changes is imperative
- Personal items such as spoons, cups and utensils should not be shared and should be properly washed with detergent after use;
- The use of gowns may act as a useful protection for health personnel looking after these patients; and
- Patients with HFMD should be isolated and the usual isolation procedures followed for infection control.

3.3 Patients with neurologic complication

Huang et al reviewed HFMD cases in Taiwan in 1998 and they found that the mean age of patients with neurological manifestations was 2.5 (range, 3 months to 8.2 years[10]. Higher incidence occurs in the younger age group. The neurologic disorders usually began 2 to 5 days after the onset of skin or mucosa lesion or fever.

Wu JM et al carried out a prospective study among infants confirmed to have enterovirus 71 and found that[11];

- EV71 infection can lead to severe neurologic complications and acute pulmonary edema with or without hemorrhage
- All patients with EV71 infection and pulmonary edema had brainstem lesions
- Viral myocarditis is not the direct cause of acute PE and cardiopulmonary failure in EV71 Infection
- The excessive central sympathetic activation resulting in vasoconstriction was not the major cause of PE or hemorrhage

Based on the findings, they suggested that;

- Vasodilators should be used with caution since pulmonary edema in EV71 infection is not resulting from excessive vasoconstriction alone
- Cardiopulmonary function usually returns to nearly normal within days but the neurogic sequelae are severe and usually permanent. Therefore the use of extracorporeal membrane oxygenation support or a heart assist device should be weighed carefully
- Direct intracardiac hemodynamic monitoring may provide additional information to guide critical care

3.4. ADVICE GIVEN UPON PATIENT'S DISCHARGE

Parents and guardians should be advised upon patients discharge on complications that may occur; a statement as shown below can be given:

> "Your child has been diagnosed to have hand-foot-mouth disease. This disease is normally not dangerous but in the light of recent events, we advise that you bring back your child to this hospital if he / she has any of the following symptoms:
>
> - High fever.
> - Lethargy and weakness.
> - Refusing feeds and passing less urine.
> - Rapid breathing.
> - Vomiting.
> - Drowsiness or irritably.
> - Fits."

4. SURVEILLANCE

The actual burden of HFMD in this country is not known. HFMD surveillance in Malaysia started after the Sarawak outbreak in 1997 with sentinel surveillance. Both private and government clinics were included as sentinel sites for each district. The number of sentinel sites for each district depends on the assumed prevalence of HFMD in the district / state.

HFMD notification is administratively required and started since October 2005. However death of HFMD and admitted cases to the ward of children aged 10 years old and below is mandatory for notification. However due to frequent outbreaks and fatality in Sarawak, Sarawak State has required all HFMD cases in the state to be notified.

The notification of HFMD came into enforcement on 12 October 2006 under the PU.A 374 / 2006 (appendix 1).

3.1 Objective of surveillance

i. To detect impending outbreak.
ii. To monitor circulating infectious agent.
iii. To estimate the magnitude of HFMD in the population at risk.
iv. To estimate the magnitude of the HFMD complication in the population at risk.

3.2 Case definition

3.2.1 Clinical case definition

3.2.1.1 Case of HFMD:

Any child with:

a. mouth / tongue ulcer **and**
b. maculopapular rashes and / **or** vesicles on palms and soles
c. **with OR without** history of fever

3.2.1.2 HFMD myocarditis:

2(i) **Suspected HFMD myocarditis**

Asymptomatic child with unexplained tachycardia to fulminant congestive cardiac failure.

With history of dirrhoea or URTI.

Accompanied by fever, malaise, tachypnoea, tachycardia (above and beyond expected for age and fever) or dehydration.

Pallor and shock in the absence of or obvious pulmonary sign or in the presence of crepitations (no murmurs) and / or a clinically enlarged heart.

2(i) **Confirmed HFMD myocarditis**.

The above 2(i) with virologic confirmation of enteroviruses.

3.2.1.3 HFMD meningoencephalitis / AFP

3(i) **Suspected HFMD meningoencephalitis**

Evidence of aseptic meningitis.

Evidence of aseptic encephalitis.

Evidence of AFP.

3(ii) **Confirmed HFMD meningoencephalitis / AFP.**

The above 3(i) with virologic confirmation of enteroviruses

3.2.2 Laboratory criteria

Any case that has the clinical symptoms and positive for viruses (coxsackieviruses (Cox) A16, A5, A9, A10, B2, B5 and enterovirus (EV) 71) which could cause HFMD, isolated or detected from stool or vesicle fluid or mouth ulcer or saliva.

3.2.3 Case classification

Suspected: A case that meets the clinical case definition.

Confirmed: A suspected case in which laboratory investigation confirms the presence of virus OR when cases are epidemiologically linked to a laboratory confirmed case.

3.3 Types of surveillance

3.3.1 Clinical surveillance

It is mandatory to notify HFMD under the National Notification of Infectious Diseases (list of notifiable diseases). Notification must be done within 24 hours of diagnosis via telephone, then it should be followed by notification form.

All HFMD cases detected must be entered to CDCIS. If states have other methods of data storing, it must be shared with MOH.

Laboratory confirmation is **NOT** required for notification.

3.2.2 Laboratory surveillance

Sentinel sites

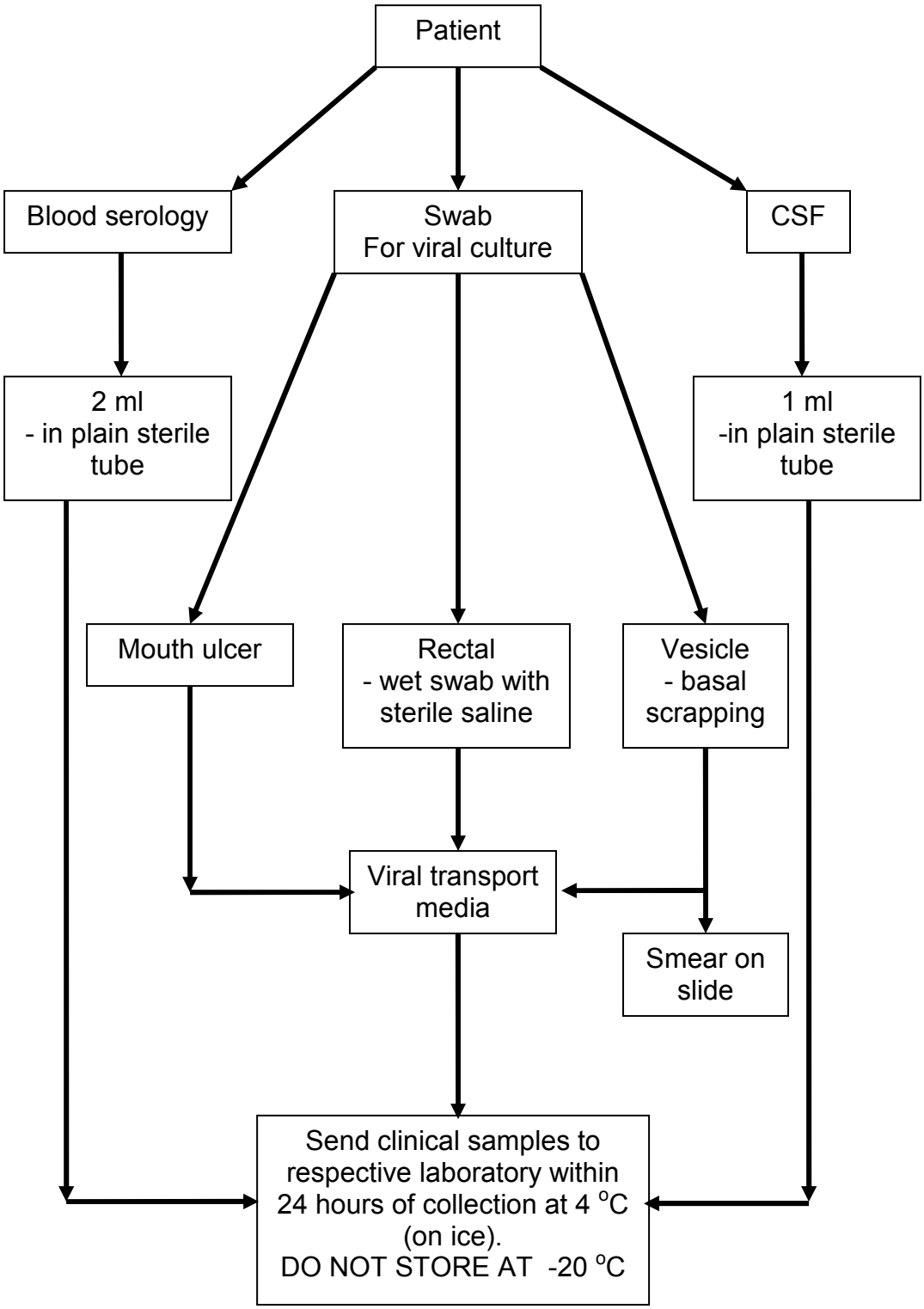
Enterovirus surveillance is done through state's sentinel sites. A state has to choose two sentinel sites. Preferably the sites have a considerable numbers of children cases as HFMD prevalence is higher among this age group. At least 5 specimens from 5 patients per centre should be taken and sent to the designated laboratory (as in table below). Please use the laboratory request form as in appendix 2(i).

Designated laboratory involves in enterovirus surveillance

Laboratory	Contact number	Respective states
IMR	03-26988792	Johor, WPKL, Melaka, Terengganu, Pahang.
UMMC	03-79675756 / 79676678	Selangor.
NPHL	03-61402213	Perlis, Kedah, Perak, Penang
HUKM	03 - 91702203 / 2208	Negeri Sembilan
USM	09 - 7664602 / 4609 / 3000 ext 4602	Kelantan

Surveillance for Sarawak and Sabah is expected to start once Kota Kinabalu Public Health Laboratory is ready to function.

Clinical Specimen Collection, Handling And Transportation

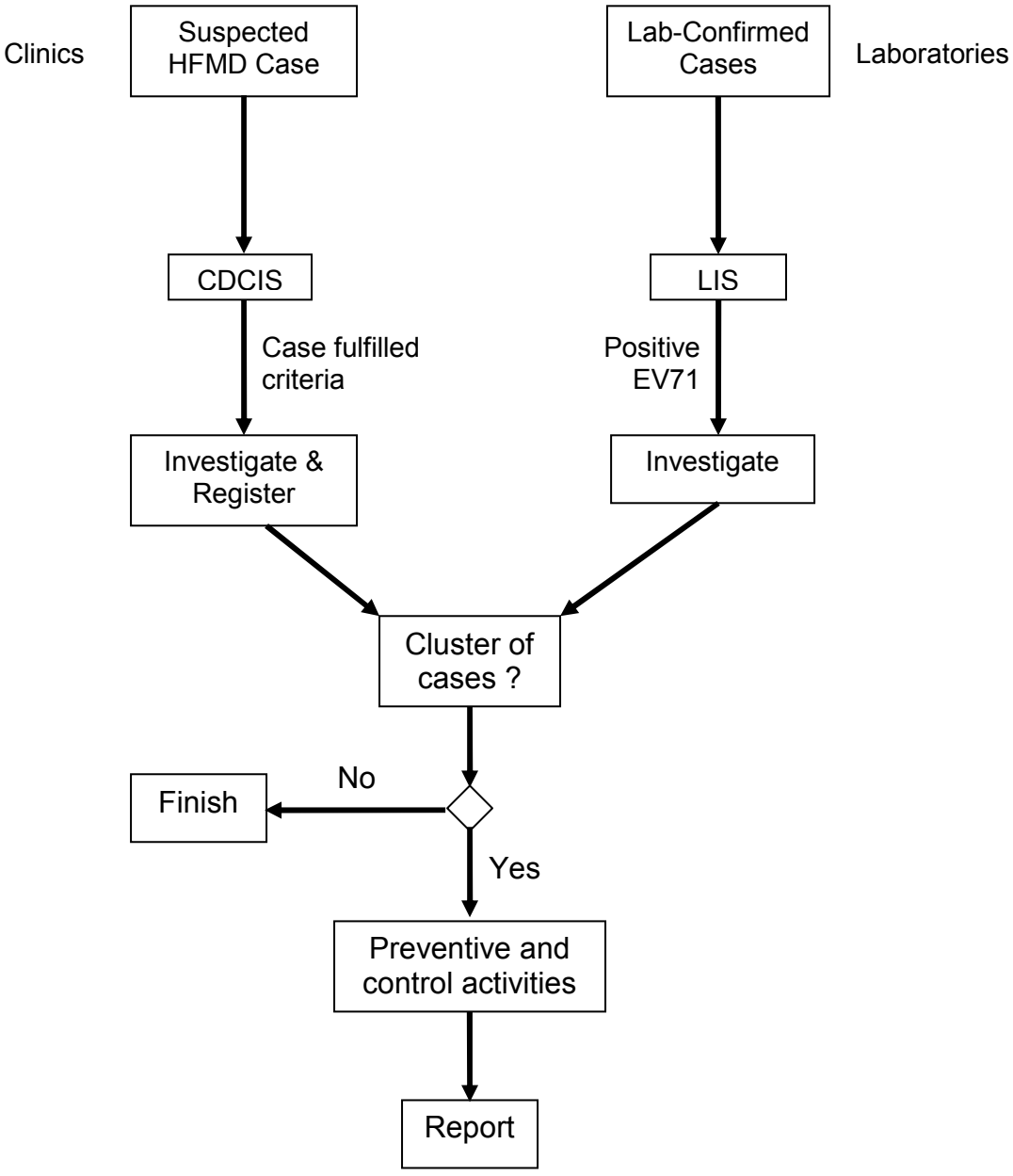


3.4 Flow of surveillance data

Notification data should be entered in CDCIS as and when there is HFMD case. Other sources of data must be shared with Disease Control Division. Data must have the variables listed in appendix 1.

Laboratory results for enterovirus surveillance must be shared with respective states and Disease Control Division using the suggested format in appendix 2(ii).

Flow of Information Management



5. MANAGEMENT OF SPORADIC CASES

5.1 Definitions of sporadic case:

A single case of HFMD in the absence of previous known close contact with another case.

5.2 The public health measures

5.2.1 Case Investigation

Case investigation is required following the criteria below:

a. every notified HFMD case that fulfilled any one of the criteria below:

   i. case is admitted to hospital
   ii. case died.
   iii. case aged 6 years and below **and** goes to any pre-schools or nurseries.

The first two criteria indicate severity of illness and it is a proxy of possible EV71 infection. Meanwhile the third criterion is important in preventing spread of illness among the pre-school children (high risk group) and reducing public anxiety.

b. every case with positive EV71 laboratory result.

Investigation should be carried out to determine the course, source and severity of infection. Enquiries shall be made into;

1. Particulars of the person affected
2. Clinical signs and symptoms with date of onset. In addition, enquiries shall be elicited for associated complications e.g. seizures, weakness of limbs, staring episodes, drowsiness, profound lethargy and refusal to play.

   Enterovirus infections that are not associated with complications may not have cutaneous manifestations.
3. Duration of illness
4. Type of treatment sought, including details of hospitalization and reason for admission
5. History of travel especially to outbreak area in the past two weeks
6. Contacts with similar illness in an institution (child care centre or kindergarten), family or neighbourhood where relevant.
7. If newborn, antenatal history including maternal history of febrile illness, mode of delivery

5.2.2 Incidence management

Following steps should be taken to prevent further spread of disease / pathogen:

1. Ensure that the infected children remain away from the institution for at least ten days after onset of symptoms and must be certified free from infection by a registered medical practitioner prior to returning to school.
2. Active case detection shall be carried out among contacts in the institution and family, and all those with illness shall be referred for treatment at the nearest health clinics.
3. Swabs from oral ulcers and vesicular lesions on the hands and feet shall be collected for virus isolation at identified laboratories (IMR or NPHL). If these ulcers and vesicles are no longer present, stool specimens shall be sent. Always consult pathologist for specimens taking, handling and transportation.
4. Health education of supervisors of institutions on the disease, mode of transmission, importance of good personal hygiene and isolation of infected children shall be carried out.
5. Principals, teachers and supervisors shall be alerted to look out for children with fever, rash / blisters on palms and soles and to isolate them immediately. Screening before coming to class is recommended (please refer *Buku Panduan Latihan Taska dan Prasekolah*).
6. If there are two or case in the premise, advice the premise to be closed to cut disease transmission. It should be closed for two incubation period (10 days) from the date of onset of the last case.
7. Supervision on disinfection procedures shall be given to the premise operators. Articles such as toys contaminated by infected cases are disinfected with 0.5% sodium hypochlorite solutions (please refer *Buku Panduan Latihan Taska dan Prasekolah*).

6. MANAGEMENT OF OUTBREAK

6.1 Definitions of outbreak

The occurrence of two or more cases in the same locality within the incubation period.

Organisation based outbreak – two or more cases with onset in two weeks interval in a group which makes epidemiological sense.

6.2 Identification of outbreaks

Surveillance data on HFMD cases should be reviewed on continuous basis to identify cases and detects outbreaks.

6.3 Risk factors for outbreaks

Risk factors for outbreaks are not completely understood. A combination of conditions (environment, host and organism) is necessary for an epidemic to occur. However large HFMD outbreaks have been associated with EV71 infection.

6.4 Management of outbreaks

When a suspected outbreak is reported, it is important to determine rapidly whether a true outbreak is occurring based on the definition above.

Similar steps as in sporadic case management should be carried out together with following measures;

1. Ensure that the infected children remain away from the institution for at least ten days after onset of symptoms and must be certified free from infection by a registered medical practitioner prior to returning to school.
2. An assessment of the number of cases and susceptible population involved shall be made, and the overall attack rate and age-specific attack rate computed.
3. Active case detection shall be carried out among contacts in the institution and family, and all those with illness shall be referred for treatment at the nearest health clinics.
4. Where a case is observed or suspected to have unusual signs and symptoms e.g. seizures, weakness of limbs, profound lethargy, refusal to play, the case shall be immediately referred to hospital.
5. Swabs from oral ulcers and vesicular lesions on the hands and feet shall be collected for virus isolation at identified laboratories (IMR or NPHL). If these ulcers and vesicles are no longer present, stool specimens shall be sent. Always consult pathologist for specimens taking, handling and transportation.

6. Principals, teachers and supervisors shall be alerted to look out for children with fever, rash / blisters on palms and soles and to isolate them immediately. Screening before coming to class is recommended (please refer *Buku Panduan Latihan Taska dan Prasekolah*).
7. Health education of supervisors of institutions on the disease, mode of transmission, importance of good personal hygiene and isolation of infected children shall be carried out.
8. Close the premise closed for two incubation period (10 days) from the date of onset of the last case. Supervision on disinfection procedures shall be given to the premise operators.

In addition the investigating team shall also look into environmental sanitation and hygiene to ensure that:

a. Articles such as toys contaminated by infected cases are disinfected with 0.5% sodium hypochlorite solutions (please refer *Buku Panduan Latihan Taska dan Prasekolah*).
b. A high standard of food and personal hygiene is maintained by the institution involved which include proper waste and diapers disposal.
c. The approved enrolment of Department of Social Welfare (JKM), Ministry of Education, Department of National Integration and other relevant parties, where applicable, and shall notify the relevant authorities if regulations not complied.

If the outbreak occurs in primary schools;

i. Ensure that the infected students remain away from the institution for at least ten days.
ii. Health education to the students on the disease, mode of transmission, importance of good personal hygiene.
iii. Principals, teachers and supervisors shall be look for children with fever, rash / blisters on palms and soles and to isolate them immediately. Screening before coming to class is recommended (please refer *Buku Panduan Latihan Taska dan Prasekolah*).
iv. If closure is necessary, just closed the affected class. Closure of the whole school is unnecessary as HFMD in older children is usually very mild and so far no complication has been documented from this agegroup.

6.5 Documentation and review

Disease activity and emergency response should be adequately documented so that further outbreaks can be handled more effectively. A summary report should be prepared within a month from the last date of case; and distributed to all the stakeholders for feedback. Format of report, dissemination and tabling of report is discussed in more details in Infectious Disease Outbreak Rapid Response Manual.[12]

Appendix 1

Variables required in HFMD surveillance database

1 Epid week
2 Name
3 Age
4 Sex
5 Ethnic
6 Home address
7 Locality
8 District
9 Name of school / preschool / nursery
10 Address of school / preschool / nursery
11 Date of onset
12 Case definition fulfilled
13 Symptoms and signs of CNS
14 Contact with HFMD case
15 Address of contact
16 Date of seen
17 Name of clinic / hospital
18 Government or private health facility
19 Outpatient or inpatient treatment
20 Date of admitted
21 Date of discharge
22 Date of death

Appendix 2(i)

No. Rujukan Makmal	

NATIONAL ENTEROVIRUS SURVEILLANCE
DIAGNOSTIC REQUEST FORM

A. MAKLUMAT PESAKIT		
Negeri :	Daerah :	
Hospital (wad) / Klinik Kesihatan		No. R/N :
Nama Pesakit :		
No. K/P :	Umur :	Jantina : L / P
Bangsa :	Tarikh lahir :	

B. MAKLUMAT KLINIKAL		
Gejala (Simptom)	Ada / Tiada (Tandakan √)	Tarikh mula
Demam > 38 ^{0}C		
Ulser di mulut & tekak		
Maculopapular rashes dan / Vesikel pada tapak tangan dan tapak kaki		
Tanda dan gejala URTI		

C. SPESIMEN KLINIKAL			
Spesimen		**Tarikh diambil**	**Tarikh penghantaran**
Rectal swab		/ /	/ /
Mouth ulcer		/ /	/ /
Vesicle swab		/ /	/ /
Stool		/ /	/ /

D. MAKLUMAT PEMOHON	
Nama dan Cop Pegawai : Tandatangan :	No. telefon : No. fax : e-mail :

E. MAKMAL (Untuk Kegunaan Makmal)			
Keadaan spesimen :			Tarikh terima spesimen :
Spesimen	**Jenis ujian**	**Keputusan ujian**	**Komen**
Rectal swab			
Mouth ulcer			
Vesicle swab			
Stool			

Nama dan tandatangan Pegawai Makmal :	
Jawatan Pegawai Makmal dan Cop Makmal :	Tarikh :

Nota * : All samples except blood / serum and stool must be in the viral transport media (VTM) and send immediately in ice pack to HUKM Microbiological Laboratory.

Appendix 2(ii)

Variables Required for Enterovirus Surveillance Database

Name of Centre / Laboratory: _____

No	Date Sample Received	Date Sample Collected	LN	RN	Name	Ethnic	Age	Sex	Source	Case diagnosis	Type of spec	Result		
												IF	Isolation	PCR

BORANG SIASATAN PESAKIT DI WAD
PENYAKIT TANGAN, KAKI DAN MULUT (HFMD)
BAHAGIAN KAWALAN PENYAKIT, KEMENTERIAN KESIHATAN MALAYSIA

BAHAGIAN 1

Tarikh masuk wad: ☐☐☐☐☐☐ Masa: ☐☐☐☐

Tarikh discaj: ☐☐☐☐☐☐ Masa: ☐☐☐☐

Tarikh kematian ☐☐☐☐☐☐ Masa: ☐☐☐☐

A. PERIHAL PESAKIT

1. Nama pesakit:
2. Tarikh lahir: ☐☐☐☐☐☐
3. Nama ibu:
4. No K/P ibu:
5. Alamat rumah:
6. No telefon: (rumah)
(H/P)

Kedudukan rumah (GPS): X : _____ Y : _____

7. Jantina: ☐ Lelaki ☐ Perempuan

8. Kumpulan etnik
☐ Melayu ☐ Kadazan/Dusun
☐ Cina ☐ Murut
☐ India ☐ Bajau
☐ Asli semenanjung ☐ Melanau
☐ Bidayuh ☐ Iban
☐ Lain-lain pribumi ☐ Lain-lain (nyatakan) Sabah/ Sarawak

9. Kewarganegaraan: ☐ Malaysia ☐ Warga asing

10. Menghadiri sekolah / taska
☐ Ya
☐ Taska / Nurseri
☐ Prasekolah
☐ Sekolah
Nyatakan nama: _____
☐ Tidak

B. MAKLUMAT KLINIKAL

1. Tarikh mula sakit (onset) ☐☐☐☐☐☐☐☐

2. Tanda dan gejala: Ya ☐ Tidak ☐
Riwayat demam

Ulser mulut	☐	☐
Ruam (rash) tapak tangan / kaki	☐	☐
vesicles di tapak tangan / kaki	☐	☐

3. Kompliksi	Ya	Tidak
Aseptic meningitis	☐	☐
Myocarditis	☐	☐
Encephalitis	☐	☐
Acute flaccid paralysis	☐	☐
Jika ya, sila nyatakan bahagian anggota: _____		
Kematian	☐	☐

C. MAKLUMAT UJIAN MAKMAL

SAMPEL	Tarikh diambil	Keputusan	Tarikh keputusan
Throat swab			
Rectal swab			
Vesicle swab			
Stool			
Blood			
CSF			
Biopsy _____ (Nyatakan tisu)			

D. MAKLUMAT PEGAWAI YANG MERAWAT

1. Nama Pakar / Pegawai Perubatan: _____ Tandatangan: _____
2. Nama Wad: _____
3. Nama hospital: _____ Tarikh notifikasi: _____

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HAND FOOT AND MOUTH DISEASE (HFMD) GUIDELINES

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1. INTRODUCTION

Hand foot and mouth disease (HFMD) is typically a benign and common illness among children and infants characterized by rapidly ulcerating vesicles in the mouth and lesions, usually vesicular, on the hands and feet.[1] HFMD is an endemic disease in Malaysia. HFMD has become an important public health disease due to its tendency to cause large outbreaks and deaths among children and infants. The purpose of the guidelines is to help health personnels and health authorities, at any levels;

- To update current knowledge about HFMD
- To detect and control epidemic of HFMD as early as possible
- To strengthen the capacity for emergency response to epidemics of HFMD
- To improve the outcome of HFMD cases through effective case management.

2. THE DISEASE

Hand foot and mouth disease (HFMD) is caused by systemic infections with human enteroviruses. Human enteroviruses comprise one genus in the family Picornaviridae, which also contains the genera rhinovirus, cardiovirus, aphthovirus, hepatovirus and parechovirus. The members of the enterovirus genus that infect humans include the polioviruses, the Coxsackie virus groups A and B, the echoviruses and the enteroviruses 68-71.[2]

2.1 Transmission

Hand foot and mouth disease (HFMD) is moderately contagious. Infection is spread from person to person by direct contact with nose and throat discharges, saliva, fluid from blisters, or the stool of infected persons. A person is most contagious during the first week of the illness.

2.2 Clinical Features

HFMD is characterised by vesicular eruptions on the hands, wrists, feet and within the mouth. Lesions on the hands are almost always present, but oral lesions are present in 90% of patients and can occasionally be the only manifestation of the disease. The oral vesicles are often on the palate, tongue, and buccal mucosa and may range from a few isolated lesions to a marked stomatitis.

In addition patients may suffer fever, malaise, conjunctival injection, headache, and abdominal pain and occasionally diarrhea. The lesions on the feet and hands are flaccid, grayish vesicles, most often on the sides of the fingers, instep and

toes. If the disease is confined to the oral cavity it is almost indistinguishable from primary herpetic gingivostomatitis.[3]

Hand foot and mouth disease may be related to coxsackieviruses A16, A5, A9, A10, B2, B5 and enterovirus 71. Coxsackievirus A16 (Cox A16) is a frequently encountered pathogen in cases of HFMD and its clinical course is usually uneventful, with full recovery.

Fatal cases of Cox A16 infection are rare. Literature search revealed only three fatal cases of Cox A16 since 1963. All the cases were infants. The first case was reported by Wright et al in 1963 involving a 10 month-old girl with respiratory infection.[4] The second case involved a 7 month-old boy with grunting and tongue ulcers.[5] The third case was reported by Wang et al involving a 15 month-old boy who presented with hand foot and mouth disease complicated with myocarditis and intractable shock.[6]

HFMD caused by enterovirus 71 (EV71) can be more severe and may be complicated with meningitis, encephalitis and neurogenic pulmonary edema. In Taiwan, based on 1998 epidemic, the significant difference in the clinical features of Coxsackievirus A16 infection and EV 71 infection was that in EV71 the fever was usually higher than 39°C and longer than 3 days.[7]

Enterovirus 71 infection can be classified into 4 stages:

Stage 1 – Hand foot and mouth disease (HFMD), oral ulcers and vesicular rash appearing on the hands, feet, knees and / or buttocks; or herpangina including oral ulceration over anterior tonsillar pillars, the soft palate, buccal mucosa or uvula.

Stage 2 – CNS involvement - aseptic meningitis with headache, irritability or myoclonic jerk and CSF pleocytosis (> 5 x 10^6 leucocytes / litre) but without altered level of consciousness and focal signs, or encephalitis with altered level of consciousness plus CSF pleocytosis or poliomyelitis like syndrome with acute limb weakness and decreased reflex and muscle strength, or encephalomyelitis with the occurrence of both encephalitis and poliomyelitis like syndrome.

Stage 3 – Cardiopulmonary failure, pulmonary edema or hemorrhage with decreased ejection fraction of left ventricle as assessed by echocardiography necessitating inotropic agent support.

Stage 4 – Convalescence - is defined as recovery from cardiopulmonary failure.

2.3 Magnitude of the disease

Hand foot and mouth disease (HFMD) generally is a common and self limiting disease among children. EV 71 infection is the more important public health concern. In temperate countries most HFMD cases occur in the summer and fall and the incubation period is 4 – 6 days.

EV 71 was first isolated from a child with aseptic meningitis in California in 1969, and by 1974, the virus had been described as a new serotype of genus *Enterovirus.* In the years following the initial isolation of EV71, outbreaks occurred in USA, Australia, Sweden and Japan. In 1975 EV71 gained global attention when it was responsible for an outbreak in Bulgaria that resulted in 705 cases of poliomyelitis-like disease and the deaths of 44 people; 93% of the poliomyelitis-like disease cases occurred in children under the age of five. A similar outbreak occurred in Hungary in 1978, which also involved many cases of poliomyelitis-like disease and 47 deaths. Since this time outbreaks of EV71 have continued to occur throughout the world.

More recently there has been an increase in EV71 activity in the Asia Pacific region with several epidemics of HFMD being reported, including multiple cases associated with brain stem encephalitis and pulmonary edema. The first such epidemic occurred in Sarawak (Malaysian Borneo) in 1997 followed by smaller outbreaks in peninsular Malaysia and Japan. In 1998 outbreaks continued in Singapore and Taiwan.

The outbreak that occurred in Taiwan is the largest recorded, with greater than 100,000 cases of HFMD. Of these 400 children were admitted to hospital with central nervous system (CNS) involvement and 78 died of brainstem encephalitis with neurogenic pulmonary oedema.[8] In 1999, a large HFMD outbreak occurred in Perth, western Australia and in 2000, EV71 was the cause of epidemics in Korea, Japan, Singapore, Taiwan and peninsular Malaysia, resulting in a range of clinical presentations including HFMD, aseptic meningitis, encephalitis and poliomyelitis like disease. Another outbreak occurred in Sarawak in 2003 which coincide with the SARS outbreak in the region and the public health measures put into place during this time evidently served to control transmission of enteroviruses as well.[9]

3. CLINICAL MANAGEMENT OF HFMD

HFMD is usually a mild and self limiting. In general, most cases of HFMD do not require admission but can be managed as outpatients. Most fatal HFMD cases were due to enterovirus infection.

3.1 Symptomatic treatment

Mild HFMD cases only need symptomatic treatment. Treatment of fever and relief of symptoms, adequate hydration and rest are important. Parents and care takers should be educated on hygiene and measures that they should take to prevent transmission to other children.

3.2 Hospitalisation.

3.2.1 Criteria for admission

- When the child is unable to tolerate oral feeds and there is a need for intravenous hydration;
- When the child is clinically very ill or toxic-looking
- When some other more serious disease cannot be excluded
- When there is persistent hyperpyrexia (e.g >38ºC) for >48 hours;
- When there is a suspicion of neurological complications, e.g increased lethargy, myoclonus, increased drowsiness, change in sensorium and/or seizures;
- When there is a suspicion of cardiac complications (myocarditis), e.g low blood pressure, low pulse volume, heart rhythm abnormalities, murmurs, gallop rhythm, displaced apex beat;
- When parents are unable to cope with child's illness; and
- When there is inadequate family or social support in looking after the child at home.

3.2.2 Infection control

- Proper hygiene including mandatory hand washing after contact with patient, appropriate cleanliness during diaper changes is imperative
- Personal items such as spoons, cups and utensils should not be shared and should be properly washed with detergent after use;
- The use of gowns may act as a useful protection for health personnel looking after these patients; and
- Patients with HFMD should be isolated and the usual isolation procedures followed for infection control.

3.3 Patients with neurologic complication

Huang et al reviewed HFMD cases in Taiwan in 1998 and they found that the mean age of patients with neurological manifestations was 2.5 (range, 3 months to 8.2 years[10]. Higher incidence occurs in the younger age group. The neurologic disorders usually began 2 to 5 days after the onset of skin or mucosa lesion or fever.

Wu JM et al carried out a prospective study among infants confirmed to have enterovirus 71 and found that[11];

- EV71 infection can lead to severe neurologic complications and acute pulmonary edema with or without hemorrhage
- All patients with EV71 infection and pulmonary edema had brainstem lesions
- Viral myocarditis is not the direct cause of acute PE and cardiopulmonary failure in EV71 Infection
- The excessive central sympathetic activation resulting in vasoconstriction was not the major cause of PE or hemorrhage

Based on the findings, they suggested that;

- Vasodilators should be used with caution since pulmonary edema in EV71 infection is not resulting from excessive vasoconstriction alone
- Cardiopulmonary function usually returns to nearly normal within days but the neurogic sequelae are severe and usually permanent. Therefore the use of extracorporeal membrane oxygenation support or a heart assist device should be weighed carefully
- Direct intracardiac hemodynamic monitoring may provide additional information to guide critical care

3.4. ADVICE GIVEN UPON PATIENT'S DISCHARGE

Parents and guardians should be advised upon patients discharge on complications that may occur; a statement as shown below can be given:

> "Your child has been diagnosed to have hand-foot-mouth disease. This disease is normally not dangerous but in the light of recent events, we advise that you bring back your child to this hospital if he / she has any of the following symptoms:
>
> - High fever.
> - Lethargy and weakness.
> - Refusing feeds and passing less urine.
> - Rapid breathing.
> - Vomiting.
> - Drowsiness or irritably.
> - Fits."

4. SURVEILLANCE

The actual burden of HFMD in this country is not known. HFMD surveillance in Malaysia started after the Sarawak outbreak in 1997 with sentinel surveillance. Both private and government clinics were included as sentinel sites for each district. The number of sentinel sites for each district depends on the assumed prevalence of HFMD in the district / state.

HFMD notification is administratively required and started since October 2005. However death of HFMD and admitted cases to the ward of children aged 10 years old and below is mandatory for notification. However due to frequent outbreaks and fatality in Sarawak, Sarawak State has required all HFMD cases in the state to be notified.

The notification of HFMD came into enforcement on 12 October 2006 under the PU.A 374 / 2006 (appendix 1).

3.1 Objective of surveillance

i. To detect impending outbreak.
ii. To monitor circulating infectious agent.
iii. To estimate the magnitude of HFMD in the population at risk.
iv. To estimate the magnitude of the HFMD complication in the population at risk.

3.2 Case definition

3.2.1 Clinical case definition

3.2.1.1 Case of HFMD:

Any child with:

a. mouth / tongue ulcer **and**
b. maculopapular rashes and / **or** vesicles on palms and soles
c. **with OR without** history of fever

3.2.1.2 HFMD myocarditis:

2(i) **Suspected HFMD myocarditis**

Asymptomatic child with unexplained tachycardia to fulminant congestive cardiac failure.

With history of dirrhoea or URTI.

Accompanied by fever, malaise, tachypnoea, tachycardia (above and beyond expected for age and fever) or dehydration.

Pallor and shock in the absence of or obvious pulmonary sign or in the presence of crepitations (no murmurs) and / or a clinically enlarged heart.

2(i) **Confirmed HFMD myocarditis**.

The above 2(i) with virologic confirmation of enteroviruses.

3.2.1.3 HFMD meningoencephalitis / AFP

3(i) **Suspected HFMD meningoencephalitis**

Evidence of aseptic meningitis.

Evidence of aseptic encephalitis.

Evidence of AFP.

3(ii) **Confirmed HFMD meningoencephalitis / AFP.**

The above 3(i) with virologic confirmation of enteroviruses

3.2.2 Laboratory criteria

Any case that has the clinical symptoms and positive for viruses (coxsackieviruses (Cox) A16, A5, A9, A10, B2, B5 and enterovirus (EV) 71) which could cause HFMD, isolated or detected from stool or vesicle fluid or mouth ulcer or saliva.

3.2.3 Case classification

Suspected: A case that meets the clinical case definition.

Confirmed: A suspected case in which laboratory investigation confirms the presence of virus OR when cases are epidemiologically linked to a laboratory confirmed case.

3.3 Types of surveillance

3.3.1 Clinical surveillance

It is mandatory to notify HFMD under the National Notification of Infectious Diseases (list of notifiable diseases). Notification must be done within 24 hours of diagnosis via telephone, then it should be followed by notification form.

All HFMD cases detected must be entered to CDCIS. If states have other methods of data storing, it must be shared with MOH.

Laboratory confirmation is **NOT** required for notification.

3.2.2 Laboratory surveillance

Sentinel sites

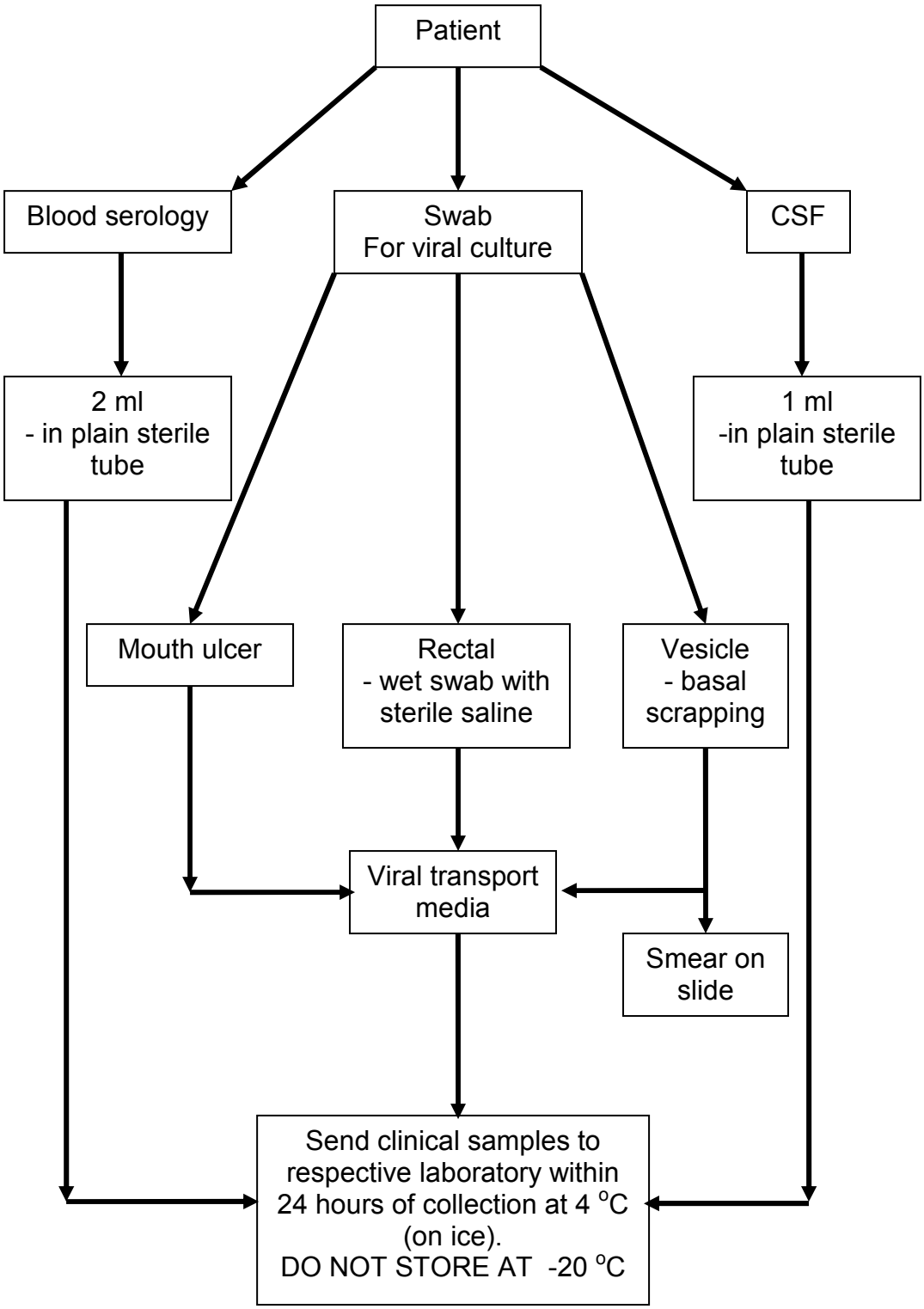
Enterovirus surveillance is done through state's sentinel sites. A state has to choose two sentinel sites. Preferably the sites have a considerable numbers of children cases as HFMD prevalence is higher among this age group. At least 5 specimens from 5 patients per centre should be taken and sent to the designated laboratory (as in table below). Please use the laboratory request form as in appendix 2(i).

Designated laboratory involves in enterovirus surveillance

Laboratory	Contact number	Respective states
IMR	03-26988792	Johor, WPKL, Melaka, Terengganu, Pahang.
UMMC	03-79675756 / 79676678	Selangor.
NPHL	03-61402213	Perlis, Kedah, Perak, Penang
'HUKM	03 - 91702203 / 2208	Negeri Sembilan
USM	09 - 7664602 / 4609 / 3000 ext 4602	Kelantan

Surveillance for Sarawak and Sabah is expected to start once Kota Kinabalu Public Health Laboratory is ready to function.

Clinical Specimen Collection, Handling And Transportation

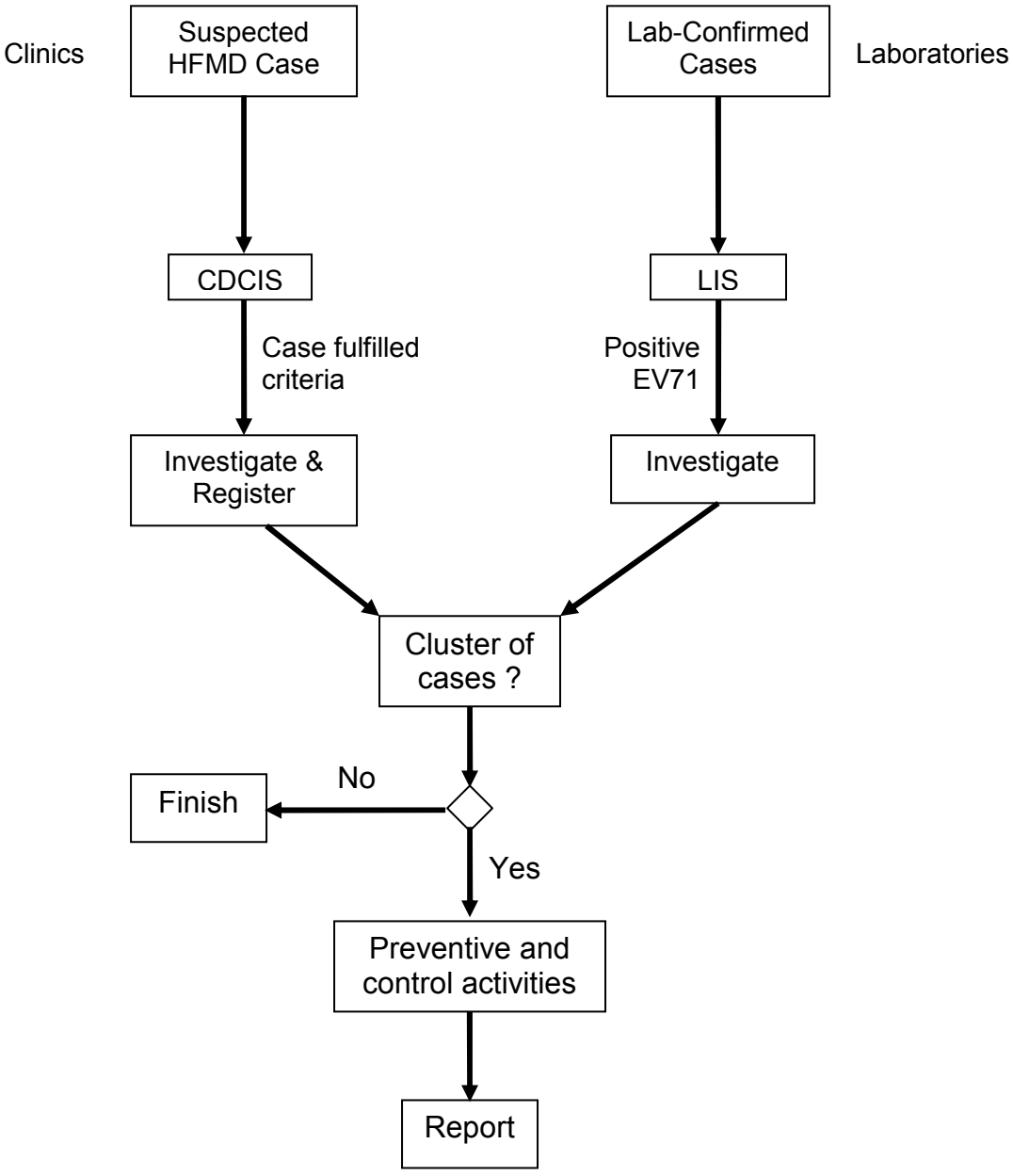


3.4 Flow of surveillance data

Notification data should be entered in CDCIS as and when there is HFMD case. Other sources of data must be shared with Disease Control Division. Data must have the variables listed in appendix 1.

Laboratory results for enterovirus surveillance must be shared with respective states and Disease Control Division using the suggested format in appendix 2(ii).

Flow of Information Management



5. MANAGEMENT OF SPORADIC CASES

5.1 Definitions of sporadic case:

A single case of HFMD in the absence of previous known close contact with another case.

5.2 The public health measures

5.2.1 Case Investigation

Case investigation is required following the criteria below:

a. every notified HFMD case that fulfilled any one of the criteria below:

   i. case is admitted to hospital
   ii. case died.
   iii. case aged 6 years and below **and** goes to any pre-schools or nurseries.

The first two criteria indicate severity of illness and it is a proxy of possible EV71 infection. Meanwhile the third criterion is important in preventing spread of illness among the pre-school children (high risk group) and reducing public anxiety.

b. every case with positive EV71 laboratory result.

Investigation should be carried out to determine the course, source and severity of infection. Enquiries shall be made into;

1. Particulars of the person affected
2. Clinical signs and symptoms with date of onset. In addition, enquiries shall be elicited for associated complications e.g. seizures, weakness of limbs, staring episodes, drowsiness, profound lethargy and refusal to play.

   Enterovirus infections that are not associated with complications may not have cutaneous manifestations.
3. Duration of illness
4. Type of treatment sought, including details of hospitalization and reason for admission
5. History of travel especially to outbreak area in the past two weeks
6. Contacts with similar illness in an institution (child care centre or kindergarten), family or neighbourhood where relevant.
7. If newborn, antenatal history including maternal history of febrile illness, mode of delivery

5.2.2 Incidence management

Following steps should be taken to prevent further spread of disease / pathogen:

1. Ensure that the infected children remain away from the institution for at least ten days after onset of symptoms and must be certified free from infection by a registered medical practitioner prior to returning to school.
2. Active case detection shall be carried out among contacts in the institution and family, and all those with illness shall be referred for treatment at the nearest health clinics.
3. Swabs from oral ulcers and vesicular lesions on the hands and feet shall be collected for virus isolation at identified laboratories (IMR or NPHL). If these ulcers and vesicles are no longer present, stool specimens shall be sent. Always consult pathologist for specimens taking, handling and transportation.
4. Health education of supervisors of institutions on the disease, mode of transmission, importance of good personal hygiene and isolation of infected children shall be carried out.
5. Principals, teachers and supervisors shall be alerted to look out for children with fever, rash / blisters on palms and soles and to isolate them immediately. Screening before coming to class is recommended (please refer *Buku Panduan Latihan Taska dan Prasekolah*).
6. If there are two or case in the premise, advice the premise to be closed to cut disease transmission. It should be closed for two incubation period (10 days) from the date of onset of the last case.
7. Supervision on disinfection procedures shall be given to the premise operators. Articles such as toys contaminated by infected cases are disinfected with 0.5% sodium hypochlorite solutions (please refer *Buku Panduan Latihan Taska dan Prasekolah*).

6. MANAGEMENT OF OUTBREAK

6.1 Definitions of outbreak

The occurrence of two or more cases in the same locality within the incubation period.

Organisation based outbreak – two or more cases with onset in two weeks interval in a group which makes epidemiological sense.

6.2 Identification of outbreaks

Surveillance data on HFMD cases should be reviewed on continuous basis to identify cases and detects outbreaks.

6.3 Risk factors for outbreaks

Risk factors for outbreaks are not completely understood. A combination of conditions (environment, host and organism) is necessary for an epidemic to occur. However large HFMD outbreaks have been associated with EV71 infection.

6.4 Management of outbreaks

When a suspected outbreak is reported, it is important to determine rapidly whether a true outbreak is occurring based on the definition above.

Similar steps as in sporadic case management should be carried out together with following measures;

1. Ensure that the infected children remain away from the institution for at least ten days after onset of symptoms and must be certified free from infection by a registered medical practitioner prior to returning to school.
2. An assessment of the number of cases and susceptible population involved shall be made, and the overall attack rate and age-specific attack rate computed.
3. Active case detection shall be carried out among contacts in the institution and family, and all those with illness shall be referred for treatment at the nearest health clinics.
4. Where a case is observed or suspected to have unusual signs and symptoms e.g. seizures, weakness of limbs, profound lethargy, refusal to play, the case shall be immediately referred to hospital.
5. Swabs from oral ulcers and vesicular lesions on the hands and feet shall be collected for virus isolation at identified laboratories (IMR or NPHL). If these ulcers and vesicles are no longer present, stool specimens shall be sent. Always consult pathologist for specimens taking, handling and transportation.

6. Principals, teachers and supervisors shall be alerted to look out for children with fever, rash / blisters on palms and soles and to isolate them immediately. Screening before coming to class is recommended (please refer *Buku Panduan Latihan Taska dan Prasekolah*).
7. Health education of supervisors of institutions on the disease, mode of transmission, importance of good personal hygiene and isolation of infected children shall be carried out.
8. Close the premise closed for two incubation period (10 days) from the date of onset of the last case. Supervision on disinfection procedures shall be given to the premise operators.

In addition the investigating team shall also look into environmental sanitation and hygiene to ensure that:

a. Articles such as toys contaminated by infected cases are disinfected with 0.5% sodium hypochlorite solutions (please refer *Buku Panduan Latihan Taska dan Prasekolah*).
b. A high standard of food and personal hygiene is maintained by the institution involved which include proper waste and diapers disposal.
c. The approved enrolment of Department of Social Welfare (JKM), Ministry of Education, Department of National Integration and other relevant parties, where applicable, and shall notify the relevant authorities if regulations not complied.

If the outbreak occurs in primary schools;

i. Ensure that the infected students remain away from the institution for at least ten days.
ii. Health education to the students on the disease, mode of transmission, importance of good personal hygiene.
iii. Principals, teachers and supervisors shall be look for children with fever, rash / blisters on palms and soles and to isolate them immediately. Screening before coming to class is recommended (please refer *Buku Panduan Latihan Taska dan Prasekolah*).
iv. If closure is necessary, just closed the affected class. Closure of the whole school is unnecessary as HFMD in older children is usually very mild and so far no complication has been documented from this agegroup.

6.5 Documentation and review

Disease activity and emergency response should be adequately documented so that further outbreaks can be handled more effectively. A summary report should be prepared within a month from the last date of case; and distributed to all the stakeholders for feedback. Format of report, dissemination and tabling of report is discussed in more details in Infectious Disease Outbreak Rapid Response Manual.[12]

Appendix 1

Variables required in HFMD surveillance database

1 Epid week
2 Name
3 Age
4 Sex
5 Ethnic
6 Home address
7 Locality
8 District
9 Name of school / preschool / nursery
10 Address of school / preschool / nursery
11 Date of onset
12 Case definition fulfilled
13 Symptoms and signs of CNS
14 Contact with HFMD case
15 Address of contact
16 Date of seen
17 Name of clinic / hospital
18 Government or private health facility
19 Outpatient or inpatient treatment
20 Date of admitted
21 Date of discharge
22 Date of death

Appendix 2(i)

No. Rujukan Makmal	

NATIONAL ENTEROVIRUS SURVEILLANCE
DIAGNOSTIC REQUEST FORM

A. MAKLUMAT PESAKIT		
Negeri :	Daerah :	
Hospital (wad) / Klinik Kesihatan		No. R/N :
Nama Pesakit :		
No. K/P :	Umur :	Jantina : L / P
Bangsa :	Tarikh lahir :	

B. MAKLUMAT KLINIKAL		
Gejala (Simptom)	Ada / Tiada (Tandakan √)	Tarikh mula
Demam > 38 ^{0}C		
Ulser di mulut & tekak		
Maculopapular rashes dan / Vesikel pada tapak tangan dan tapak kaki		
Tanda dan gejala URTI		

C. SPESIMEN KLINIKAL			
Spesimen		**Tarikh diambil**	**Tarikh penghantaran**
Rectal swab		/ /	/ /
Mouth ulcer		/ /	/ /
Vesicle swab		/ /	/ /
Stool		/ /	/ /

D. MAKLUMAT PEMOHON	
Nama dan Cop Pegawai : Tandatangan :	No. telefon : No. fax : e-mail :

E. MAKMAL (Untuk Kegunaan Makmal)			
Keadaan spesimen :			Tarikh terima spesimen :
Spesimen	**Jenis ujian**	**Keputusan ujian**	**Komen**
Rectal swab			
Mouth ulcer			
Vesicle swab			
Stool			

Nama dan tandatangan Pegawai Makmal :	
Jawatan Pegawai Makmal dan Cop Makmal :	Tarikh :

Nota * : All samples except blood / serum and stool must be in the viral transport media (VTM) and send immediately in ice pack to HUKM Microbiological Laboratory.

Appendix 2(ii)

Variables Required for Enterovirus Surveillance Database

Name of Centre / Laboratory: _____

No	Date Sample Received	Date Sample Collected	LN	RN	Name	Ethnic	Age	Sex	Source	Case diagnosis	Type of spec	Result		
												IF	Isolation	PCR

BORANG SIASATAN PESAKIT DI WAD
PENYAKIT TANGAN, KAKI DAN MULUT (HFMD)
BAHAGIAN KAWALAN PENYAKIT, KEMENTERIAN KESIHATAN MALAYSIA

BAHAGIAN 1

Tarikh masuk wad: ☐☐☐☐☐☐ Masa: ☐☐☐☐

Tarikh discaj: ☐☐☐☐☐☐ Masa: ☐☐☐☐

Tarikh kematian ☐☐☐☐☐☐ Masa: ☐☐☐☐

A. PERIHAL PESAKIT

1. Nama pesakit:
2. Tarikh lahir: ☐☐☐☐☐☐
3. Nama ibu:
4. No K/P ibu:
5. Alamat rumah:
6. No telefon: (rumah)
(H/P)

Kedudukan rumah (GPS): X : _____ Y : _____

7. Jantina: ☐ Lelaki ☐ Perempuan

8. Kumpulan etnik
☐ Melayu ☐ Kadazan/Dusun
☐ Cina ☐ Murut
☐ India ☐ Bajau
☐ Asli semenanjung ☐ Melanau
☐ Bidayuh ☐ Iban
☐ Lain-lain pribumi ☐ Lain-lain (nyatakan) Sabah/ Sarawak

9. Kewarganegaraan: ☐ Malaysia ☐ Warga asing

10. Menghadiri sekolah / taska
☐ Ya
☐ Taska / Nurseri
☐ Prasekolah
☐ Sekolah
Nyatakan nama: _____
☐ Tidak

B. MAKLUMAT KLINIKAL

1. Tarikh mula sakit (onset) ☐☐☐☐☐☐☐☐

2. Tanda dan gejala: Ya ☐ Tidak ☐
Riwayat demam

Ulser mulut	☐	☐
Ruam (rash) tapak tangan / kaki	☐	☐
vesicles di tapak tangan / kaki	☐	☐

3. Kompliksi	Ya	Tidak
Aseptic meningitis	☐	☐
Myocarditis	☐	☐
Encephalitis	☐	☐
Acute flaccid paralysis	☐	☐
Jika ya, sila nyatakan bahagian anggota: _____		
Kematian	☐	☐

C. MAKLUMAT UJIAN MAKMAL

SAMPEL	Tarikh diambil	Keputusan	Tarikh keputusan
Throat swab			
Rectal swab			
Vesicle swab			
Stool			
Blood			
CSF			
Biopsy _____ (Nyatakan tisu)			

D. MAKLUMAT PEGAWAI YANG MERAWAT

1. Nama Pakar / Pegawai Perubatan: _____ Tandatangan: _____
2. Nama Wad: _____
3. Nama hospital: _____ Tarikh notifikasi: _____

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HAND FOOT AND MOUTH DISEASE (HFMD) GUIDELINES

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1. INTRODUCTION

Hand foot and mouth disease (HFMD) is typically a benign and common illness among children and infants characterized by rapidly ulcerating vesicles in the mouth and lesions, usually vesicular, on the hands and feet.[1] HFMD is an endemic disease in Malaysia. HFMD has become an important public health disease due to its tendency to cause large outbreaks and deaths among children and infants. The purpose of the guidelines is to help health personnels and health authorities, at any levels;

- To update current knowledge about HFMD
- To detect and control epidemic of HFMD as early as possible
- To strengthen the capacity for emergency response to epidemics of HFMD
- To improve the outcome of HFMD cases through effective case management.

2. THE DISEASE

Hand foot and mouth disease (HFMD) is caused by systemic infections with human enteroviruses. Human enteroviruses comprise one genus in the family Picornaviridae, which also contains the genera rhinovirus, cardiovirus, aphthovirus, hepatovirus and parechovirus. The members of the enterovirus genus that infect humans include the polioviruses, the Coxsackie virus groups A and B, the echoviruses and the enteroviruses 68-71.[2]

2.1 Transmission

Hand foot and mouth disease (HFMD) is moderately contagious. Infection is spread from person to person by direct contact with nose and throat discharges, saliva, fluid from blisters, or the stool of infected persons. A person is most contagious during the first week of the illness.

2.2 Clinical Features

HFMD is characterised by vesicular eruptions on the hands, wrists, feet and within the mouth. Lesions on the hands are almost always present, but oral lesions are present in 90% of patients and can occasionally be the only manifestation of the disease. The oral vesicles are often on the palate, tongue, and buccal mucosa and may range from a few isolated lesions to a marked stomatitis.

In addition patients may suffer fever, malaise, conjunctival injection, headache, and abdominal pain and occasionally diarrhea. The lesions on the feet and hands are flaccid, grayish vesicles, most often on the sides of the fingers, instep and

toes. If the disease is confined to the oral cavity it is almost indistinguishable from primary herpetic gingivostomatitis.[3]

Hand foot and mouth disease may be related to coxsackieviruses A16, A5, A9, A10, B2, B5 and enterovirus 71. Coxsackievirus A16 (Cox A16) is a frequently encountered pathogen in cases of HFMD and its clinical course is usually uneventful, with full recovery.

Fatal cases of Cox A16 infection are rare. Literature search revealed only three fatal cases of Cox A16 since 1963. All the cases were infants. The first case was reported by Wright et al in 1963 involving a 10 month-old girl with respiratory infection.[4] The second case involved a 7 month-old boy with grunting and tongue ulcers.[5] The third case was reported by Wang et al involving a 15 month-old boy who presented with hand foot and mouth disease complicated with myocarditis and intractable shock.[6]

HFMD caused by enterovirus 71 (EV71) can be more severe and may be complicated with meningitis, encephalitis and neurogenic pulmonary edema. In Taiwan, based on 1998 epidemic, the significant difference in the clinical features of Coxsackievirus A16 infection and EV 71 infection was that in EV71 the fever was usually higher than 39°C and longer than 3 days.[7]

Enterovirus 71 infection can be classified into 4 stages:

Stage 1 – Hand foot and mouth disease (HFMD), oral ulcers and vesicular rash appearing on the hands, feet, knees and / or buttocks; or herpangina including oral ulceration over anterior tonsillar pillars, the soft palate, buccal mucosa or uvula.

Stage 2 – CNS involvement - aseptic meningitis with headache, irritability or myoclonic jerk and CSF pleocytosis (> 5 x 10^6 leucocytes / litre) but without altered level of consciousness and focal signs, or encephalitis with altered level of consciousness plus CSF pleocytosis or poliomyelitis like syndrome with acute limb weakness and decreased reflex and muscle strength, or encephalomyelitis with the occurrence of both encephalitis and poliomyelitis like syndrome.

Stage 3 – Cardiopulmonary failure, pulmonary edema or hemorrhage with decreased ejection fraction of left ventricle as assessed by echocardiography necessitating inotropic agent support.

Stage 4 – Convalescence - is defined as recovery from cardiopulmonary failure.

2.3 Magnitude of the disease

Hand foot and mouth disease (HFMD) generally is a common and self limiting disease among children. EV 71 infection is the more important public health concern. In temperate countries most HFMD cases occur in the summer and fall and the incubation period is 4 – 6 days.

EV 71 was first isolated from a child with aseptic meningitis in California in 1969, and by 1974, the virus had been described as a new serotype of genus *Enterovirus.* In the years following the initial isolation of EV71, outbreaks occurred in USA, Australia, Sweden and Japan. In 1975 EV71 gained global attention when it was responsible for an outbreak in Bulgaria that resulted in 705 cases of poliomyelitis-like disease and the deaths of 44 people; 93% of the poliomyelitis-like disease cases occurred in children under the age of five. A similar outbreak occurred in Hungary in 1978, which also involved many cases of poliomyelitis-like disease and 47 deaths. Since this time outbreaks of EV71 have continued to occur throughout the world.

More recently there has been an increase in EV71 activity in the Asia Pacific region with several epidemics of HFMD being reported, including multiple cases associated with brain stem encephalitis and pulmonary edema. The first such epidemic occurred in Sarawak (Malaysian Borneo) in 1997 followed by smaller outbreaks in peninsular Malaysia and Japan. In 1998 outbreaks continued in Singapore and Taiwan.

The outbreak that occurred in Taiwan is the largest recorded, with greater than 100,000 cases of HFMD. Of these 400 children were admitted to hospital with central nervous system (CNS) involvement and 78 died of brainstem encephalitis with neurogenic pulmonary oedema.[8] In 1999, a large HFMD outbreak occurred in Perth, western Australia and in 2000, EV71 was the cause of epidemics in Korea, Japan, Singapore, Taiwan and peninsular Malaysia, resulting in a range of clinical presentations including HFMD, aseptic meningitis, encephalitis and poliomyelitis like disease. Another outbreak occurred in Sarawak in 2003 which coincide with the SARS outbreak in the region and the public health measures put into place during this time evidently served to control transmission of enteroviruses as well.[9]

3. CLINICAL MANAGEMENT OF HFMD

HFMD is usually a mild and self limiting. In general, most cases of HFMD do not require admission but can be managed as outpatients. Most fatal HFMD cases were due to enterovirus infection.

3.1 Symptomatic treatment

Mild HFMD cases only need symptomatic treatment. Treatment of fever and relief of symptoms, adequate hydration and rest are important. Parents and care takers should be educated on hygiene and measures that they should take to prevent transmission to other children.

3.2 Hospitalisation.

3.2.1 Criteria for admission

- When the child is unable to tolerate oral feeds and there is a need for intravenous hydration;
- When the child is clinically very ill or toxic-looking
- When some other more serious disease cannot be excluded
- When there is persistent hyperpyrexia (e.g >38ºC) for >48 hours;
- When there is a suspicion of neurological complications, e.g increased lethargy, myoclonus, increased drowsiness, change in sensorium and/or seizures;
- When there is a suspicion of cardiac complications (myocarditis), e.g low blood pressure, low pulse volume, heart rhythm abnormalities, murmurs, gallop rhythm, displaced apex beat;
- When parents are unable to cope with child's illness; and
- When there is inadequate family or social support in looking after the child at home.

3.2.2 Infection control

- Proper hygiene including mandatory hand washing after contact with patient, appropriate cleanliness during diaper changes is imperative
- Personal items such as spoons, cups and utensils should not be shared and should be properly washed with detergent after use;
- The use of gowns may act as a useful protection for health personnel looking after these patients; and
- Patients with HFMD should be isolated and the usual isolation procedures followed for infection control.

3.3 Patients with neurologic complication

Huang et al reviewed HFMD cases in Taiwan in 1998 and they found that the mean age of patients with neurological manifestations was 2.5 (range, 3 months to 8.2 years[10]. Higher incidence occurs in the younger age group. The neurologic disorders usually began 2 to 5 days after the onset of skin or mucosa lesion or fever.

Wu JM et al carried out a prospective study among infants confirmed to have enterovirus 71 and found that[11];

- EV71 infection can lead to severe neurologic complications and acute pulmonary edema with or without hemorrhage
- All patients with EV71 infection and pulmonary edema had brainstem lesions
- Viral myocarditis is not the direct cause of acute PE and cardiopulmonary failure in EV71 Infection
- The excessive central sympathetic activation resulting in vasoconstriction was not the major cause of PE or hemorrhage

Based on the findings, they suggested that;

- Vasodilators should be used with caution since pulmonary edema in EV71 infection is not resulting from excessive vasoconstriction alone
- Cardiopulmonary function usually returns to nearly normal within days but the neurogic sequelae are severe and usually permanent. Therefore the use of extracorporeal membrane oxygenation support or a heart assist device should be weighed carefully
- Direct intracardiac hemodynamic monitoring may provide additional information to guide critical care

3.4. ADVICE GIVEN UPON PATIENT'S DISCHARGE

Parents and guardians should be advised upon patients discharge on complications that may occur; a statement as shown below can be given:

> "Your child has been diagnosed to have hand-foot-mouth disease. This disease is normally not dangerous but in the light of recent events, we advise that you bring back your child to this hospital if he / she has any of the following symptoms:
>
> - High fever.
> - Lethargy and weakness.
> - Refusing feeds and passing less urine.
> - Rapid breathing.
> - Vomiting.
> - Drowsiness or irritably.
> - Fits."

4. SURVEILLANCE

The actual burden of HFMD in this country is not known. HFMD surveillance in Malaysia started after the Sarawak outbreak in 1997 with sentinel surveillance. Both private and government clinics were included as sentinel sites for each district. The number of sentinel sites for each district depends on the assumed prevalence of HFMD in the district / state.

HFMD notification is administratively required and started since October 2005. However death of HFMD and admitted cases to the ward of children aged 10 years old and below is mandatory for notification. However due to frequent outbreaks and fatality in Sarawak, Sarawak State has required all HFMD cases in the state to be notified.

The notification of HFMD came into enforcement on 12 October 2006 under the PU.A 374 / 2006 (appendix 1).

3.1 Objective of surveillance

i. To detect impending outbreak.
ii. To monitor circulating infectious agent.
iii. To estimate the magnitude of HFMD in the population at risk.
iv. To estimate the magnitude of the HFMD complication in the population at risk.

3.2 Case definition

3.2.1 Clinical case definition

3.2.1.1 Case of HFMD:

Any child with:

a. mouth / tongue ulcer **and**
b. maculopapular rashes and / **or** vesicles on palms and soles
c. **with OR without** history of fever

3.2.1.2 HFMD myocarditis:

2(i) **Suspected HFMD myocarditis**

Asymptomatic child with unexplained tachycardia to fulminant congestive cardiac failure.

With history of dirrhoea or URTI.

Accompanied by fever, malaise, tachypnoea, tachycardia (above and beyond expected for age and fever) or dehydration.

Pallor and shock in the absence of or obvious pulmonary sign or in the presence of crepitations (no murmurs) and / or a clinically enlarged heart.

2(i) **Confirmed HFMD myocarditis**.

The above 2(i) with virologic confirmation of enteroviruses.

3.2.1.3 HFMD meningoencephalitis / AFP

3(i) **Suspected HFMD meningoencephalitis**

Evidence of aseptic meningitis.

Evidence of aseptic encephalitis.

Evidence of AFP.

3(ii) **Confirmed HFMD meningoencephalitis / AFP.**

The above 3(i) with virologic confirmation of enteroviruses

3.2.2 Laboratory criteria

Any case that has the clinical symptoms and positive for viruses (coxsackieviruses (Cox) A16, A5, A9, A10, B2, B5 and enterovirus (EV) 71) which could cause HFMD, isolated or detected from stool or vesicle fluid or mouth ulcer or saliva.

3.2.3 Case classification

Suspected: A case that meets the clinical case definition.

Confirmed: A suspected case in which laboratory investigation confirms the presence of virus OR when cases are epidemiologically linked to a laboratory confirmed case.

3.3 Types of surveillance

3.3.1 Clinical surveillance

It is mandatory to notify HFMD under the National Notification of Infectious Diseases (list of notifiable diseases). Notification must be done within 24 hours of diagnosis via telephone, then it should be followed by notification form.

All HFMD cases detected must be entered to CDCIS. If states have other methods of data storing, it must be shared with MOH.

Laboratory confirmation is **NOT** required for notification.

3.2.2 Laboratory surveillance

Sentinel sites

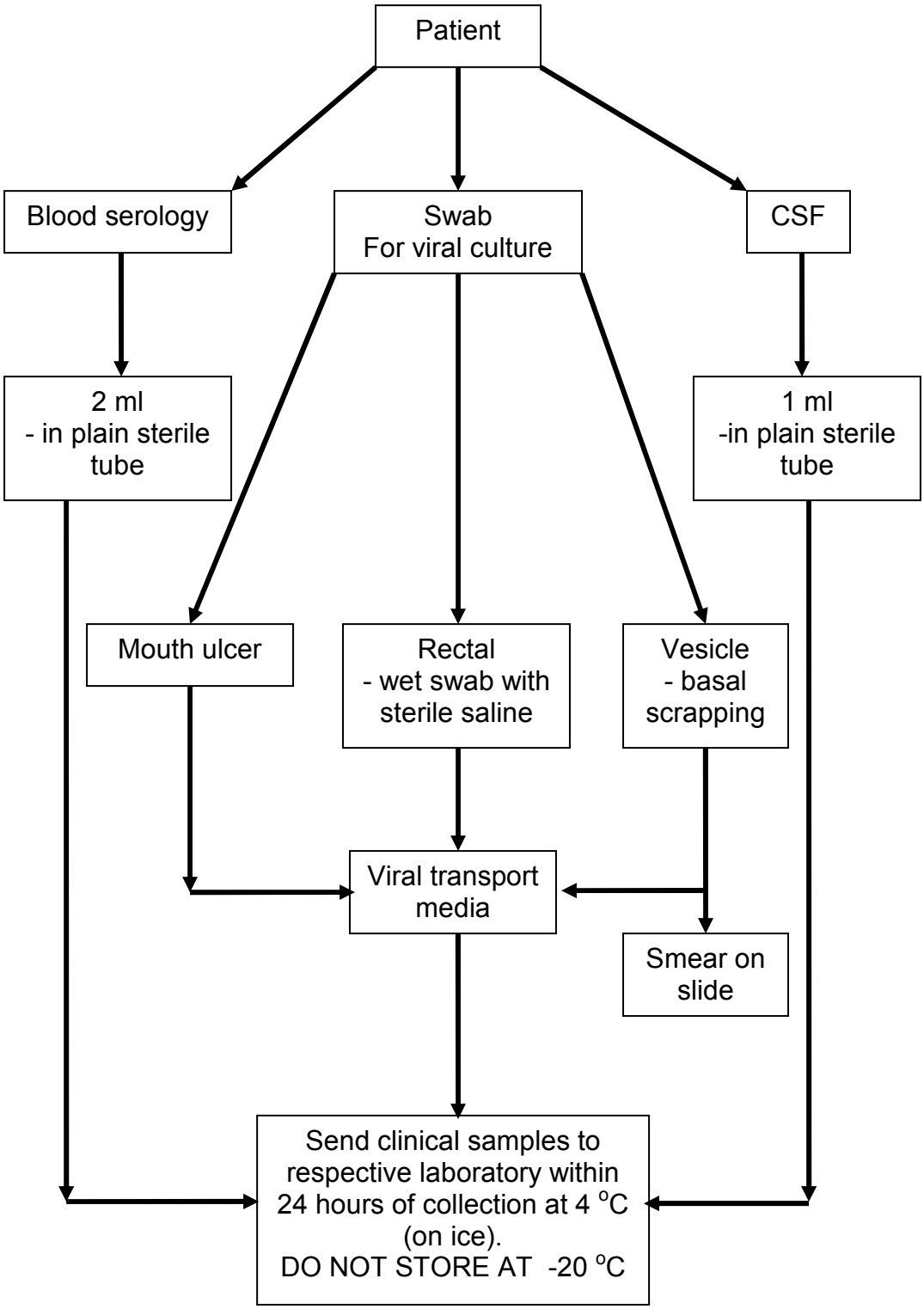
Enterovirus surveillance is done through state's sentinel sites. A state has to choose two sentinel sites. Preferably the sites have a considerable numbers of children cases as HFMD prevalence is higher among this age group. At least 5 specimens from 5 patients per centre should be taken and sent to the designated laboratory (as in table below). Please use the laboratory request form as in appendix 2(i).

Designated laboratory involves in enterovirus surveillance

Laboratory	Contact number	Respective states
IMR	03-26988792	Johor, WPKL, Melaka, Terengganu, Pahang.
UMMC	03-79675756 / 79676678	Selangor.
NPHL	03-61402213	Perlis, Kedah, Perak, Penang
'HUKM	03 - 91702203 / 2208	Negeri Sembilan
USM	09 - 7664602 / 4609 / 3000 ext 4602	Kelantan

Surveillance for Sarawak and Sabah is expected to start once Kota Kinabalu Public Health Laboratory is ready to function.

Clinical Specimen Collection, Handling And Transportation

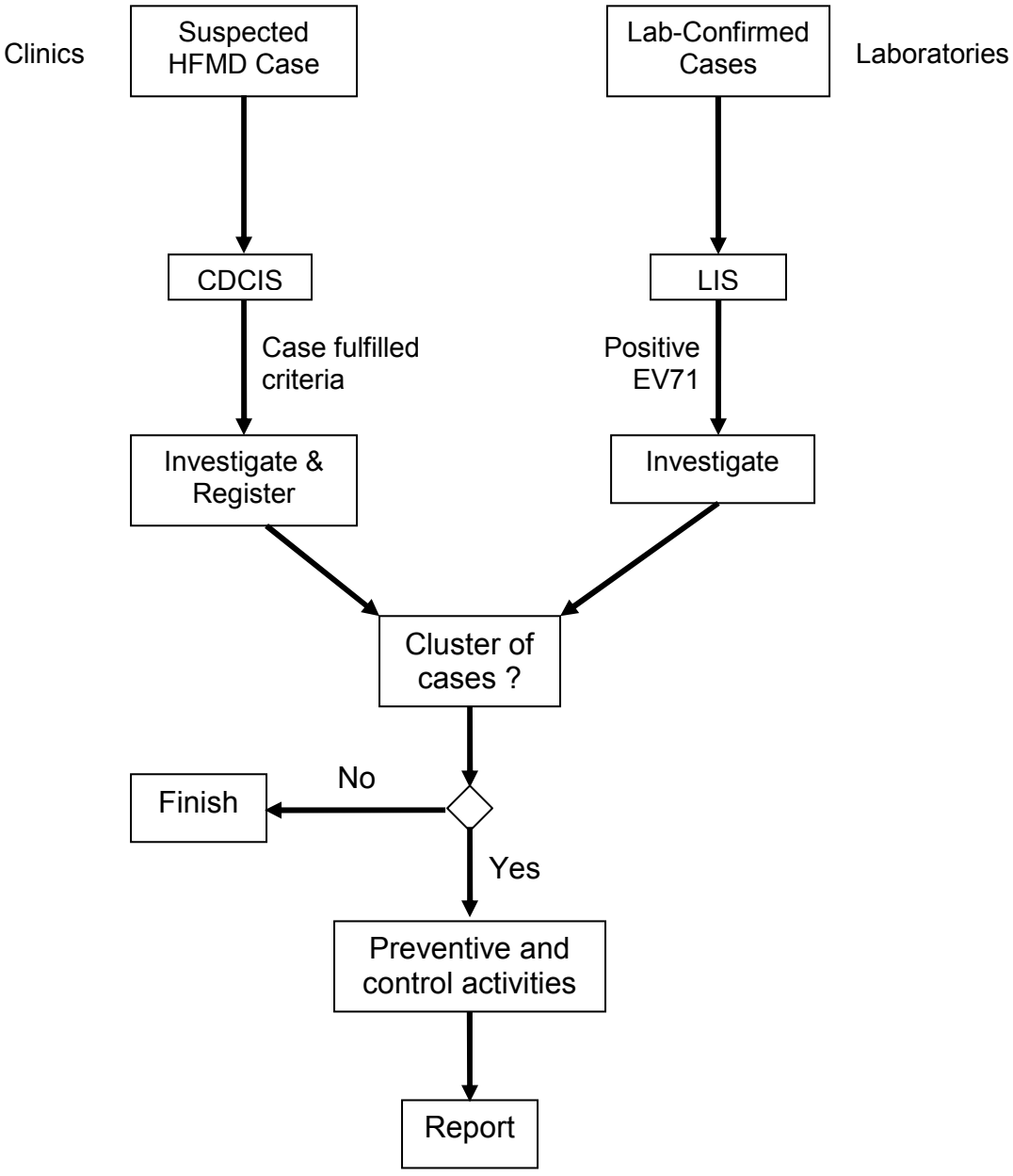


3.4 Flow of surveillance data

Notification data should be entered in CDCIS as and when there is HFMD case. Other sources of data must be shared with Disease Control Division. Data must have the variables listed in appendix 1.

Laboratory results for enterovirus surveillance must be shared with respective states and Disease Control Division using the suggested format in appendix 2(ii).

Flow of Information Management



5. MANAGEMENT OF SPORADIC CASES

5.1 Definitions of sporadic case:

A single case of HFMD in the absence of previous known close contact with another case.

5.2 The public health measures

5.2.1 Case Investigation

Case investigation is required following the criteria below:

a. every notified HFMD case that fulfilled any one of the criteria below:

   i. case is admitted to hospital
   ii. case died.
   iii. case aged 6 years and below **and** goes to any pre-schools or nurseries.

The first two criteria indicate severity of illness and it is a proxy of possible EV71 infection. Meanwhile the third criterion is important in preventing spread of illness among the pre-school children (high risk group) and reducing public anxiety.

b. every case with positive EV71 laboratory result.

Investigation should be carried out to determine the course, source and severity of infection. Enquiries shall be made into;

1. Particulars of the person affected
2. Clinical signs and symptoms with date of onset. In addition, enquiries shall be elicited for associated complications e.g. seizures, weakness of limbs, staring episodes, drowsiness, profound lethargy and refusal to play.

   Enterovirus infections that are not associated with complications may not have cutaneous manifestations.
3. Duration of illness
4. Type of treatment sought, including details of hospitalization and reason for admission
5. History of travel especially to outbreak area in the past two weeks
6. Contacts with similar illness in an institution (child care centre or kindergarten), family or neighbourhood where relevant.
7. If newborn, antenatal history including maternal history of febrile illness, mode of delivery

5.2.2 Incidence management

Following steps should be taken to prevent further spread of disease / pathogen:

1. Ensure that the infected children remain away from the institution for at least ten days after onset of symptoms and must be certified free from infection by a registered medical practitioner prior to returning to school.
2. Active case detection shall be carried out among contacts in the institution and family, and all those with illness shall be referred for treatment at the nearest health clinics.
3. Swabs from oral ulcers and vesicular lesions on the hands and feet shall be collected for virus isolation at identified laboratories (IMR or NPHL). If these ulcers and vesicles are no longer present, stool specimens shall be sent. Always consult pathologist for specimens taking, handling and transportation.
4. Health education of supervisors of institutions on the disease, mode of transmission, importance of good personal hygiene and isolation of infected children shall be carried out.
5. Principals, teachers and supervisors shall be alerted to look out for children with fever, rash / blisters on palms and soles and to isolate them immediately. Screening before coming to class is recommended (please refer *Buku Panduan Latihan Taska dan Prasekolah*).
6. If there are two or case in the premise, advice the premise to be closed to cut disease transmission. It should be closed for two incubation period (10 days) from the date of onset of the last case.
7. Supervision on disinfection procedures shall be given to the premise operators. Articles such as toys contaminated by infected cases are disinfected with 0.5% sodium hypochlorite solutions (please refer *Buku Panduan Latihan Taska dan Prasekolah*).

6. MANAGEMENT OF OUTBREAK

6.1 Definitions of outbreak

The occurrence of two or more cases in the same locality within the incubation period.

Organisation based outbreak – two or more cases with onset in two weeks interval in a group which makes epidemiological sense.

6.2 Identification of outbreaks

Surveillance data on HFMD cases should be reviewed on continuous basis to identify cases and detects outbreaks.

6.3 Risk factors for outbreaks

Risk factors for outbreaks are not completely understood. A combination of conditions (environment, host and organism) is necessary for an epidemic to occur. However large HFMD outbreaks have been associated with EV71 infection.

6.4 Management of outbreaks

When a suspected outbreak is reported, it is important to determine rapidly whether a true outbreak is occurring based on the definition above.

Similar steps as in sporadic case management should be carried out together with following measures;

1. Ensure that the infected children remain away from the institution for at least ten days after onset of symptoms and must be certified free from infection by a registered medical practitioner prior to returning to school.
2. An assessment of the number of cases and susceptible population involved shall be made, and the overall attack rate and age-specific attack rate computed.
3. Active case detection shall be carried out among contacts in the institution and family, and all those with illness shall be referred for treatment at the nearest health clinics.
4. Where a case is observed or suspected to have unusual signs and symptoms e.g. seizures, weakness of limbs, profound lethargy, refusal to play, the case shall be immediately referred to hospital.
5. Swabs from oral ulcers and vesicular lesions on the hands and feet shall be collected for virus isolation at identified laboratories (IMR or NPHL). If these ulcers and vesicles are no longer present, stool specimens shall be sent. Always consult pathologist for specimens taking, handling and transportation.

6. Principals, teachers and supervisors shall be alerted to look out for children with fever, rash / blisters on palms and soles and to isolate them immediately. Screening before coming to class is recommended (please refer *Buku Panduan Latihan Taska dan Prasekolah*).
7. Health education of supervisors of institutions on the disease, mode of transmission, importance of good personal hygiene and isolation of infected children shall be carried out.
8. Close the premise closed for two incubation period (10 days) from the date of onset of the last case. Supervision on disinfection procedures shall be given to the premise operators.

In addition the investigating team shall also look into environmental sanitation and hygiene to ensure that:

a. Articles such as toys contaminated by infected cases are disinfected with 0.5% sodium hypochlorite solutions (please refer *Buku Panduan Latihan Taska dan Prasekolah*).
b. A high standard of food and personal hygiene is maintained by the institution involved which include proper waste and diapers disposal.
c. The approved enrolment of Department of Social Welfare (JKM), Ministry of Education, Department of National Integration and other relevant parties, where applicable, and shall notify the relevant authorities if regulations not complied.

If the outbreak occurs in primary schools;

i. Ensure that the infected students remain away from the institution for at least ten days.
ii. Health education to the students on the disease, mode of transmission, importance of good personal hygiene.
iii. Principals, teachers and supervisors shall be look for children with fever, rash / blisters on palms and soles and to isolate them immediately. Screening before coming to class is recommended (please refer *Buku Panduan Latihan Taska dan Prasekolah*).
iv. If closure is necessary, just closed the affected class. Closure of the whole school is unnecessary as HFMD in older children is usually very mild and so far no complication has been documented from this agegroup.

6.5 Documentation and review

Disease activity and emergency response should be adequately documented so that further outbreaks can be handled more effectively. A summary report should be prepared within a month from the last date of case; and distributed to all the stakeholders for feedback. Format of report, dissemination and tabling of report is discussed in more details in Infectious Disease Outbreak Rapid Response Manual.[12]

Appendix 1

Variables required in HFMD surveillance database

1 Epid week
2 Name
3 Age
4 Sex
5 Ethnic
6 Home address
7 Locality
8 District
9 Name of school / preschool / nursery
10 Address of school / preschool / nursery
11 Date of onset
12 Case definition fulfilled
13 Symptoms and signs of CNS
14 Contact with HFMD case
15 Address of contact
16 Date of seen
17 Name of clinic / hospital
18 Government or private health facility
19 Outpatient or inpatient treatment
20 Date of admitted
21 Date of discharge
22 Date of death

Appendix 2(i)

No. Rujukan Makmal	

NATIONAL ENTEROVIRUS SURVEILLANCE
DIAGNOSTIC REQUEST FORM

A. MAKLUMAT PESAKIT		
Negeri :	Daerah :	
Hospital (wad) / Klinik Kesihatan		No. R/N :
Nama Pesakit :		
No. K/P :	Umur :	Jantina : L / P
Bangsa :	Tarikh lahir :	

B. MAKLUMAT KLINIKAL		
Gejala (Simptom)	Ada / Tiada (Tandakan √)	Tarikh mula
Demam > 38 ^{0}C		
Ulser di mulut & tekak		
Maculopapular rashes dan / Vesikel pada tapak tangan dan tapak kaki		
Tanda dan gejala URTI		

C. SPESIMEN KLINIKAL			
Spesimen		**Tarikh diambil**	**Tarikh penghantaran**
Rectal swab		/ /	/ /
Mouth ulcer		/ /	/ /
Vesicle swab		/ /	/ /
Stool		/ /	/ /

D. MAKLUMAT PEMOHON	
Nama dan Cop Pegawai : Tandatangan :	No. telefon : No. fax : e-mail :

E. MAKMAL (Untuk Kegunaan Makmal)			
Keadaan spesimen :			Tarikh terima spesimen :
Spesimen	**Jenis ujian**	**Keputusan ujian**	**Komen**
Rectal swab			
Mouth ulcer			
Vesicle swab			
Stool			

Nama dan tandatangan Pegawai Makmal :	
Jawatan Pegawai Makmal dan Cop Makmal :	Tarikh :

Nota * : All samples except blood / serum and stool must be in the viral transport media (VTM) and send immediately in ice pack to HUKM Microbiological Laboratory.

Appendix 2(ii)

Variables Required for Enterovirus Surveillance Database

Name of Centre / Laboratory: _____

No	Date Sample Received	Date Sample Collected	LN	RN	Name	Ethnic	Age	Sex	Source	Case diagnosis	Type of spec	Result		
												IF	Isolation	PCR

BORANG SIASATAN PESAKIT DI WAD
PENYAKIT TANGAN, KAKI DAN MULUT (HFMD)
BAHAGIAN KAWALAN PENYAKIT, KEMENTERIAN KESIHATAN MALAYSIA

BAHAGIAN 1

Tarikh masuk wad: ☐☐☐☐☐☐ Masa: ☐☐☐☐

Tarikh discaj: ☐☐☐☐☐☐ Masa: ☐☐☐☐

Tarikh kematian ☐☐☐☐☐☐ Masa: ☐☐☐☐

A. PERIHAL PESAKIT

1. Nama pesakit:
2. Tarikh lahir: ☐☐☐☐☐☐
3. Nama ibu:
4. No K/P ibu:
5. Alamat rumah:
6. No telefon: (rumah)
(H/P)

Kedudukan rumah (GPS): X : _____ Y : _____

7. Jantina: ☐ Lelaki ☐ Perempuan

8. Kumpulan etnik
☐ Melayu ☐ Kadazan/Dusun
☐ Cina ☐ Murut
☐ India ☐ Bajau
☐ Asli semenanjung ☐ Melanau
☐ Bidayuh ☐ Iban
☐ Lain-lain pribumi ☐ Lain-lain (nyatakan) Sabah/ Sarawak

9. Kewarganegaraan: ☐ Malaysia ☐ Warga asing

10. Menghadiri sekolah / taska
☐ Ya
☐ Taska / Nurseri
☐ Prasekolah
☐ Sekolah
Nyatakan nama: _____
☐ Tidak

B. MAKLUMAT KLINIKAL

1. Tarikh mula sakit (onset) ☐☐☐☐☐☐☐☐

2. Tanda dan gejala: Ya Tidak
Riwayat demam ☐ ☐

Ulser mulut	☐	☐
Ruam (rash) tapak tangan / kaki	☐	☐
vesicles di tapak tangan / kaki	☐	☐

3. Kompliksi	Ya	Tidak
Aseptic meningitis	☐	☐
Myocarditis	☐	☐
Encephalitis	☐	☐
Acute flaccid paralysis	☐	☐
Jika ya, sila nyatakan bahagian anggota: _____		
Kematian	☐	☐

C. MAKLUMAT UJIAN MAKMAL

SAMPEL	Tarikh diambil	Keputusan	Tarikh keputusan
Throat swab			
Rectal swab			
Vesicle swab			
Stool			
Blood			
CSF			
Biopsy _____ (Nyatakan tisu)			

D. MAKLUMAT PEGAWAI YANG MERAWAT

1. Nama Pakar / Pegawai Perubatan: _____ Tandatangan: _____
2. Nama Wad: _____
3. Nama hospital: _____ Tarikh notifikasi: _____

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HAND FOOT AND MOUTH DISEASE (HFMD) GUIDELINES

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1. INTRODUCTION

Hand foot and mouth disease (HFMD) is typically a benign and common illness among children and infants characterized by rapidly ulcerating vesicles in the mouth and lesions, usually vesicular, on the hands and feet.[1] HFMD is an endemic disease in Malaysia. HFMD has become an important public health disease due to its tendency to cause large outbreaks and deaths among children and infants. The purpose of the guidelines is to help health personnels and health authorities, at any levels;

- To update current knowledge about HFMD
- To detect and control epidemic of HFMD as early as possible
- To strengthen the capacity for emergency response to epidemics of HFMD
- To improve the outcome of HFMD cases through effective case management.

2. THE DISEASE

Hand foot and mouth disease (HFMD) is caused by systemic infections with human enteroviruses. Human enteroviruses comprise one genus in the family Picornaviridae, which also contains the genera rhinovirus, cardiovirus, aphthovirus, hepatovirus and parechovirus. The members of the enterovirus genus that infect humans include the polioviruses, the Coxsackie virus groups A and B, the echoviruses and the enteroviruses 68-71.[2]

2.1 Transmission

Hand foot and mouth disease (HFMD) is moderately contagious. Infection is spread from person to person by direct contact with nose and throat discharges, saliva, fluid from blisters, or the stool of infected persons. A person is most contagious during the first week of the illness.

2.2 Clinical Features

HFMD is characterised by vesicular eruptions on the hands, wrists, feet and within the mouth. Lesions on the hands are almost always present, but oral lesions are present in 90% of patients and can occasionally be the only manifestation of the disease. The oral vesicles are often on the palate, tongue, and buccal mucosa and may range from a few isolated lesions to a marked stomatitis.

In addition patients may suffer fever, malaise, conjunctival injection, headache, and abdominal pain and occasionally diarrhea. The lesions on the feet and hands are flaccid, grayish vesicles, most often on the sides of the fingers, instep and

toes. If the disease is confined to the oral cavity it is almost indistinguishable from primary herpetic gingivostomatitis.[3]

Hand foot and mouth disease may be related to coxsackieviruses A16, A5, A9, A10, B2, B5 and enterovirus 71. Coxsackievirus A16 (Cox A16) is a frequently encountered pathogen in cases of HFMD and its clinical course is usually uneventful, with full recovery.

Fatal cases of Cox A16 infection are rare. Literature search revealed only three fatal cases of Cox A16 since 1963. All the cases were infants. The first case was reported by Wright et al in 1963 involving a 10 month-old girl with respiratory infection.[4] The second case involved a 7 month-old boy with grunting and tongue ulcers.[5] The third case was reported by Wang et al involving a 15 month-old boy who presented with hand foot and mouth disease complicated with myocarditis and intractable shock.[6]

HFMD caused by enterovirus 71 (EV71) can be more severe and may be complicated with meningitis, encephalitis and neurogenic pulmonary edema. In Taiwan, based on 1998 epidemic, the significant difference in the clinical features of Coxsackievirus A16 infection and EV 71 infection was that in EV71 the fever was usually higher than 39°C and longer than 3 days.[7]

Enterovirus 71 infection can be classified into 4 stages:

Stage 1 – Hand foot and mouth disease (HFMD), oral ulcers and vesicular rash appearing on the hands, feet, knees and / or buttocks; or herpangina including oral ulceration over anterior tonsillar pillars, the soft palate, buccal mucosa or uvula.

Stage 2 – CNS involvement - aseptic meningitis with headache, irritability or myoclonic jerk and CSF pleocytosis (> 5 x 10^6 leucocytes / litre) but without altered level of consciousness and focal signs, or encephalitis with altered level of consciousness plus CSF pleocytosis or poliomyelitis like syndrome with acute limb weakness and decreased reflex and muscle strength, or encephalomyelitis with the occurrence of both encephalitis and poliomyelitis like syndrome.

Stage 3 – Cardiopulmonary failure, pulmonary edema or hemorrhage with decreased ejection fraction of left ventricle as assessed by echocardiography necessitating inotropic agent support.

Stage 4 – Convalescence - is defined as recovery from cardiopulmonary failure.

2.3 Magnitude of the disease

Hand foot and mouth disease (HFMD) generally is a common and self limiting disease among children. EV 71 infection is the more important public health concern. In temperate countries most HFMD cases occur in the summer and fall and the incubation period is 4 – 6 days.

EV 71 was first isolated from a child with aseptic meningitis in California in 1969, and by 1974, the virus had been described as a new serotype of genus *Enterovirus.* In the years following the initial isolation of EV71, outbreaks occurred in USA, Australia, Sweden and Japan. In 1975 EV71 gained global attention when it was responsible for an outbreak in Bulgaria that resulted in 705 cases of poliomyelitis-like disease and the deaths of 44 people; 93% of the poliomyelitis-like disease cases occurred in children under the age of five. A similar outbreak occurred in Hungary in 1978, which also involved many cases of poliomyelitis-like disease and 47 deaths. Since this time outbreaks of EV71 have continued to occur throughout the world.

More recently there has been an increase in EV71 activity in the Asia Pacific region with several epidemics of HFMD being reported, including multiple cases associated with brain stem encephalitis and pulmonary edema. The first such epidemic occurred in Sarawak (Malaysian Borneo) in 1997 followed by smaller outbreaks in peninsular Malaysia and Japan. In 1998 outbreaks continued in Singapore and Taiwan.

The outbreak that occurred in Taiwan is the largest recorded, with greater than 100,000 cases of HFMD. Of these 400 children were admitted to hospital with central nervous system (CNS) involvement and 78 died of brainstem encephalitis with neurogenic pulmonary oedema.[8] In 1999, a large HFMD outbreak occurred in Perth, western Australia and in 2000, EV71 was the cause of epidemics in Korea, Japan, Singapore, Taiwan and peninsular Malaysia, resulting in a range of clinical presentations including HFMD, aseptic meningitis, encephalitis and poliomyelitis like disease. Another outbreak occurred in Sarawak in 2003 which coincide with the SARS outbreak in the region and the public health measures put into place during this time evidently served to control transmission of enteroviruses as well.[9]

3. CLINICAL MANAGEMENT OF HFMD

HFMD is usually a mild and self limiting. In general, most cases of HFMD do not require admission but can be managed as outpatients. Most fatal HFMD cases were due to enterovirus infection.

3.1 Symptomatic treatment

Mild HFMD cases only need symptomatic treatment. Treatment of fever and relief of symptoms, adequate hydration and rest are important. Parents and care takers should be educated on hygiene and measures that they should take to prevent transmission to other children.

3.2 Hospitalisation.

3.2.1 Criteria for admission

- When the child is unable to tolerate oral feeds and there is a need for intravenous hydration;
- When the child is clinically very ill or toxic-looking
- When some other more serious disease cannot be excluded
- When there is persistent hyperpyrexia (e.g >38ºC) for >48 hours;
- When there is a suspicion of neurological complications, e.g increased lethargy, myoclonus, increased drowsiness, change in sensorium and/or seizures;
- When there is a suspicion of cardiac complications (myocarditis), e.g low blood pressure, low pulse volume, heart rhythm abnormalities, murmurs, gallop rhythm, displaced apex beat;
- When parents are unable to cope with child's illness; and
- When there is inadequate family or social support in looking after the child at home.

3.2.2 Infection control

- Proper hygiene including mandatory hand washing after contact with patient, appropriate cleanliness during diaper changes is imperative
- Personal items such as spoons, cups and utensils should not be shared and should be properly washed with detergent after use;
- The use of gowns may act as a useful protection for health personnel looking after these patients; and
- Patients with HFMD should be isolated and the usual isolation procedures followed for infection control.

3.3 Patients with neurologic complication

Huang et al reviewed HFMD cases in Taiwan in 1998 and they found that the mean age of patients with neurological manifestations was 2.5 (range, 3 months to 8.2 years[10]. Higher incidence occurs in the younger age group. The neurologic disorders usually began 2 to 5 days after the onset of skin or mucosa lesion or fever.

Wu JM et al carried out a prospective study among infants confirmed to have enterovirus 71 and found that[11];

- EV71 infection can lead to severe neurologic complications and acute pulmonary edema with or without hemorrhage
- All patients with EV71 infection and pulmonary edema had brainstem lesions
- Viral myocarditis is not the direct cause of acute PE and cardiopulmonary failure in EV71 Infection
- The excessive central sympathetic activation resulting in vasoconstriction was not the major cause of PE or hemorrhage

Based on the findings, they suggested that;

- Vasodilators should be used with caution since pulmonary edema in EV71 infection is not resulting from excessive vasoconstriction alone
- Cardiopulmonary function usually returns to nearly normal within days but the neurogic sequelae are severe and usually permanent. Therefore the use of extracorporeal membrane oxygenation support or a heart assist device should be weighed carefully
- Direct intracardiac hemodynamic monitoring may provide additional information to guide critical care

3.4. ADVICE GIVEN UPON PATIENT'S DISCHARGE

Parents and guardians should be advised upon patients discharge on complications that may occur; a statement as shown below can be given:

> "Your child has been diagnosed to have hand-foot-mouth disease. This disease is normally not dangerous but in the light of recent events, we advise that you bring back your child to this hospital if he / she has any of the following symptoms:
>
> - High fever.
> - Lethargy and weakness.
> - Refusing feeds and passing less urine.
> - Rapid breathing.
> - Vomiting.
> - Drowsiness or irritably.
> - Fits."

4. SURVEILLANCE

The actual burden of HFMD in this country is not known. HFMD surveillance in Malaysia started after the Sarawak outbreak in 1997 with sentinel surveillance. Both private and government clinics were included as sentinel sites for each district. The number of sentinel sites for each district depends on the assumed prevalence of HFMD in the district / state.

HFMD notification is administratively required and started since October 2005. However death of HFMD and admitted cases to the ward of children aged 10 years old and below is mandatory for notification. However due to frequent outbreaks and fatality in Sarawak, Sarawak State has required all HFMD cases in the state to be notified.

The notification of HFMD came into enforcement on 12 October 2006 under the PU.A 374 / 2006 (appendix 1).

3.1 Objective of surveillance

i. To detect impending outbreak.
ii. To monitor circulating infectious agent.
iii. To estimate the magnitude of HFMD in the population at risk.
iv. To estimate the magnitude of the HFMD complication in the population at risk.

3.2 Case definition

3.2.1 Clinical case definition

3.2.1.1 Case of HFMD:

Any child with:

a. mouth / tongue ulcer **and**
b. maculopapular rashes and / **or** vesicles on palms and soles
c. **with OR without** history of fever

3.2.1.2 HFMD myocarditis:

2(i) **Suspected HFMD myocarditis**

Asymptomatic child with unexplained tachycardia to fulminant congestive cardiac failure.

With history of dirrhoea or URTI.

Accompanied by fever, malaise, tachypnoea, tachycardia (above and beyond expected for age and fever) or dehydration.

Pallor and shock in the absence of or obvious pulmonary sign or in the presence of crepitations (no murmurs) and / or a clinically enlarged heart.

2(i) **Confirmed HFMD myocarditis**.

The above 2(i) with virologic confirmation of enteroviruses.

3.2.1.3 HFMD meningoencephalitis / AFP

3(i) **Suspected HFMD meningoencephalitis**

Evidence of aseptic meningitis.

Evidence of aseptic encephalitis.

Evidence of AFP.

3(ii) **Confirmed HFMD meningoencephalitis / AFP.**

The above 3(i) with virologic confirmation of enteroviruses

3.2.2 Laboratory criteria

Any case that has the clinical symptoms and positive for viruses (coxsackieviruses (Cox) A16, A5, A9, A10, B2, B5 and enterovirus (EV) 71) which could cause HFMD, isolated or detected from stool or vesicle fluid or mouth ulcer or saliva.

3.2.3 Case classification

Suspected: A case that meets the clinical case definition.

Confirmed: A suspected case in which laboratory investigation confirms the presence of virus OR when cases are epidemiologically linked to a laboratory confirmed case.

3.3 Types of surveillance

3.3.1 Clinical surveillance

It is mandatory to notify HFMD under the National Notification of Infectious Diseases (list of notifiable diseases). Notification must be done within 24 hours of diagnosis via telephone, then it should be followed by notification form.

All HFMD cases detected must be entered to CDCIS. If states have other methods of data storing, it must be shared with MOH.

Laboratory confirmation is **NOT** required for notification.

3.2.2 Laboratory surveillance

Sentinel sites

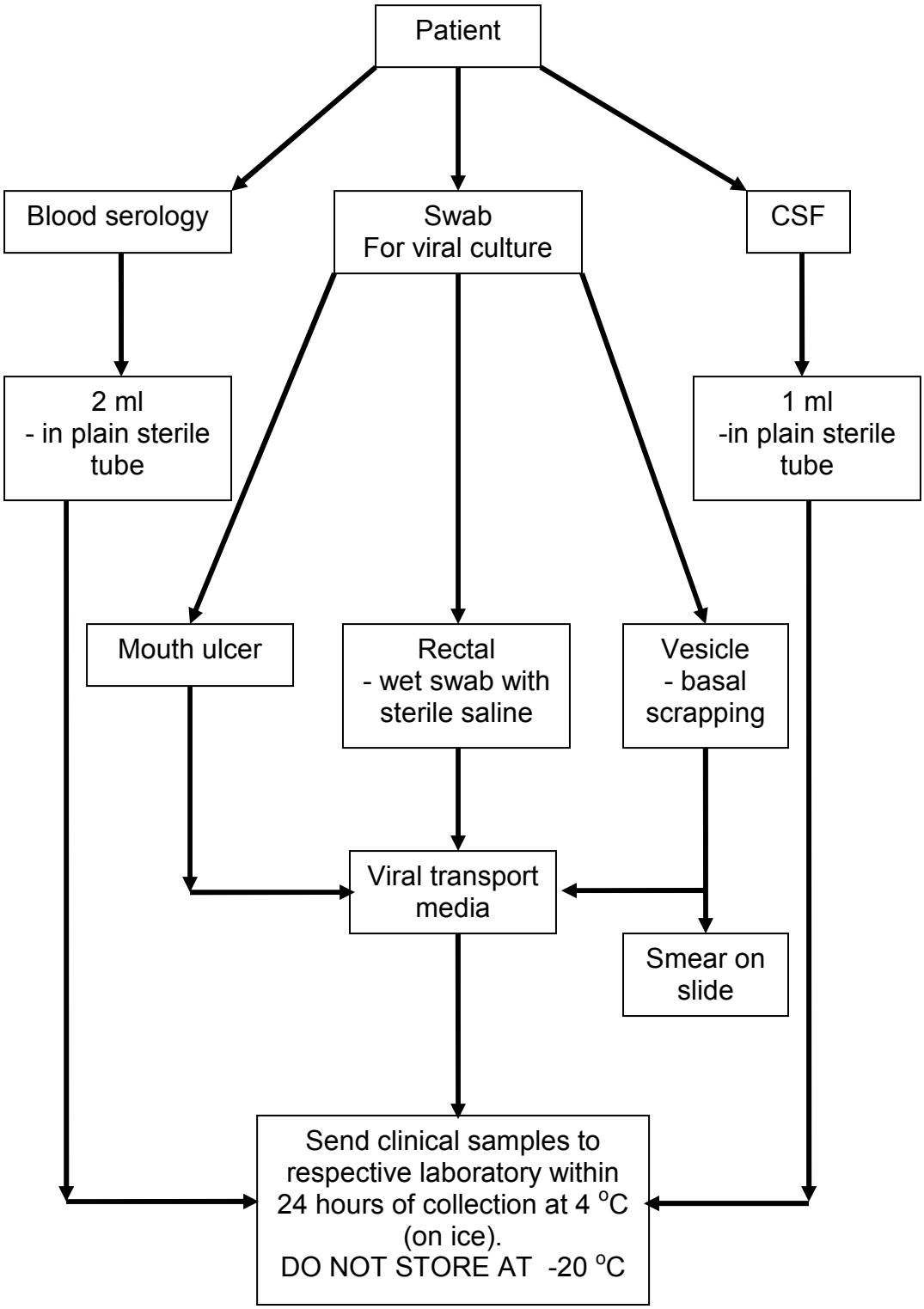
Enterovirus surveillance is done through state's sentinel sites. A state has to choose two sentinel sites. Preferably the sites have a considerable numbers of children cases as HFMD prevalence is higher among this age group. At least 5 specimens from 5 patients per centre should be taken and sent to the designated laboratory (as in table below). Please use the laboratory request form as in appendix 2(i).

Designated laboratory involves in enterovirus surveillance

Laboratory	Contact number	Respective states
IMR	03-26988792	Johor, WPKL, Melaka, Terengganu, Pahang.
UMMC	03-79675756 / 79676678	Selangor.
NPHL	03-61402213	Perlis, Kedah, Perak, Penang
'HUKM	03 - 91702203 / 2208	Negeri Sembilan
USM	09 - 7664602 / 4609 / 3000 ext 4602	Kelantan

Surveillance for Sarawak and Sabah is expected to start once Kota Kinabalu Public Health Laboratory is ready to function.

Clinical Specimen Collection, Handling And Transportation

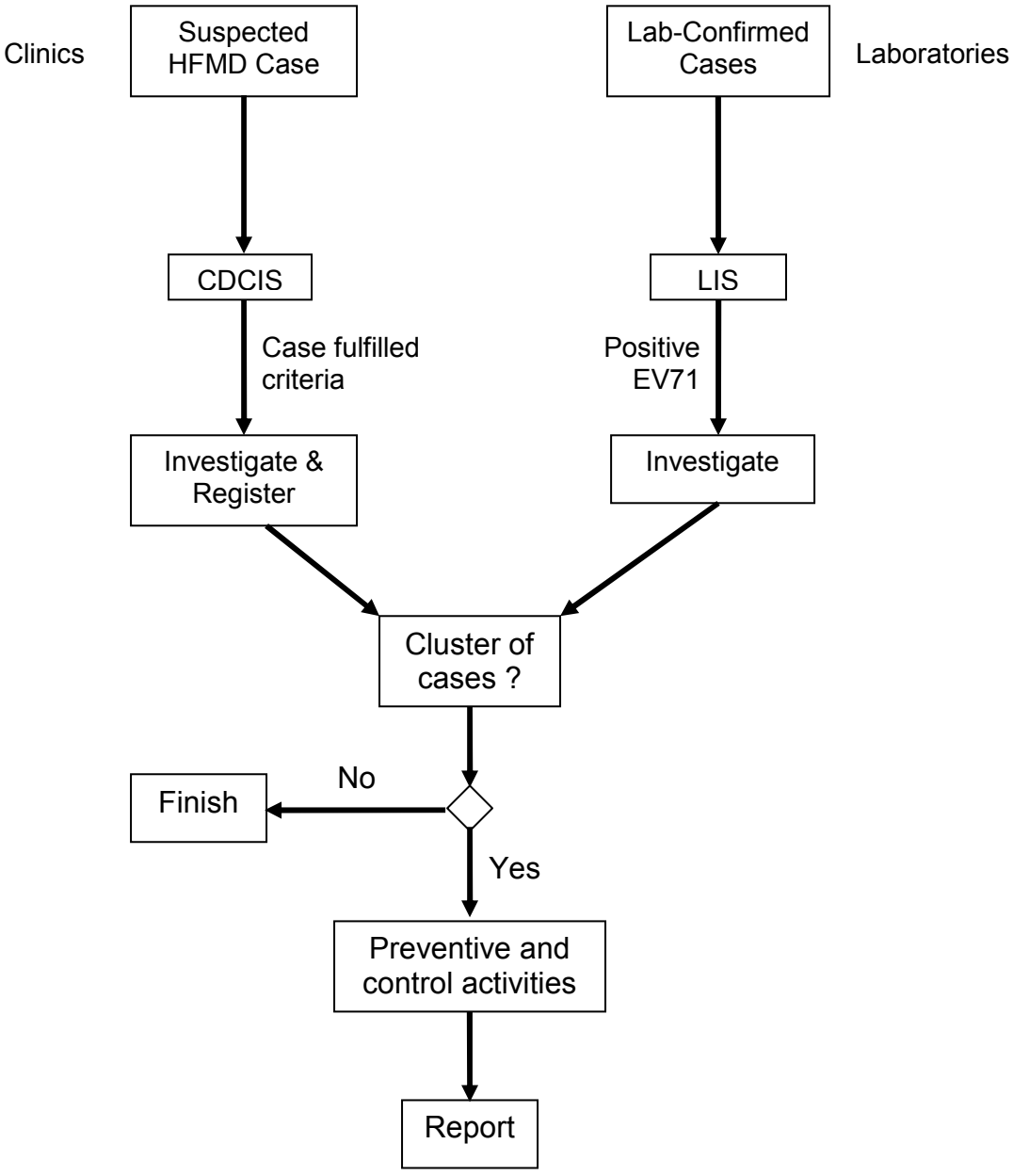


3.4 Flow of surveillance data

Notification data should be entered in CDCIS as and when there is HFMD case. Other sources of data must be shared with Disease Control Division. Data must have the variables listed in appendix 1.

Laboratory results for enterovirus surveillance must be shared with respective states and Disease Control Division using the suggested format in appendix 2(ii).

Flow of Information Management



5. MANAGEMENT OF SPORADIC CASES

5.1 Definitions of sporadic case:

A single case of HFMD in the absence of previous known close contact with another case.

5.2 The public health measures

5.2.1 Case Investigation

Case investigation is required following the criteria below:

a. every notified HFMD case that fulfilled any one of the criteria below:

   i. case is admitted to hospital
   ii. case died.
   iii. case aged 6 years and below **and** goes to any pre-schools or nurseries.

The first two criteria indicate severity of illness and it is a proxy of possible EV71 infection. Meanwhile the third criterion is important in preventing spread of illness among the pre-school children (high risk group) and reducing public anxiety.

b. every case with positive EV71 laboratory result.

Investigation should be carried out to determine the course, source and severity of infection. Enquiries shall be made into;

1. Particulars of the person affected
2. Clinical signs and symptoms with date of onset. In addition, enquiries shall be elicited for associated complications e.g. seizures, weakness of limbs, staring episodes, drowsiness, profound lethargy and refusal to play.

   Enterovirus infections that are not associated with complications may not have cutaneous manifestations.
3. Duration of illness
4. Type of treatment sought, including details of hospitalization and reason for admission
5. History of travel especially to outbreak area in the past two weeks
6. Contacts with similar illness in an institution (child care centre or kindergarten), family or neighbourhood where relevant.
7. If newborn, antenatal history including maternal history of febrile illness, mode of delivery

5.2.2 Incidence management

Following steps should be taken to prevent further spread of disease / pathogen:

1. Ensure that the infected children remain away from the institution for at least ten days after onset of symptoms and must be certified free from infection by a registered medical practitioner prior to returning to school.
2. Active case detection shall be carried out among contacts in the institution and family, and all those with illness shall be referred for treatment at the nearest health clinics.
3. Swabs from oral ulcers and vesicular lesions on the hands and feet shall be collected for virus isolation at identified laboratories (IMR or NPHL). If these ulcers and vesicles are no longer present, stool specimens shall be sent. Always consult pathologist for specimens taking, handling and transportation.
4. Health education of supervisors of institutions on the disease, mode of transmission, importance of good personal hygiene and isolation of infected children shall be carried out.
5. Principals, teachers and supervisors shall be alerted to look out for children with fever, rash / blisters on palms and soles and to isolate them immediately. Screening before coming to class is recommended (please refer *Buku Panduan Latihan Taska dan Prasekolah*).
6. If there are two or case in the premise, advice the premise to be closed to cut disease transmission. It should be closed for two incubation period (10 days) from the date of onset of the last case.
7. Supervision on disinfection procedures shall be given to the premise operators. Articles such as toys contaminated by infected cases are disinfected with 0.5% sodium hypochlorite solutions (please refer *Buku Panduan Latihan Taska dan Prasekolah*).

6. MANAGEMENT OF OUTBREAK

6.1 Definitions of outbreak

The occurrence of two or more cases in the same locality within the incubation period.

Organisation based outbreak – two or more cases with onset in two weeks interval in a group which makes epidemiological sense.

6.2 Identification of outbreaks

Surveillance data on HFMD cases should be reviewed on continuous basis to identify cases and detects outbreaks.

6.3 Risk factors for outbreaks

Risk factors for outbreaks are not completely understood. A combination of conditions (environment, host and organism) is necessary for an epidemic to occur. However large HFMD outbreaks have been associated with EV71 infection.

6.4 Management of outbreaks

When a suspected outbreak is reported, it is important to determine rapidly whether a true outbreak is occurring based on the definition above.

Similar steps as in sporadic case management should be carried out together with following measures;

1. Ensure that the infected children remain away from the institution for at least ten days after onset of symptoms and must be certified free from infection by a registered medical practitioner prior to returning to school.
2. An assessment of the number of cases and susceptible population involved shall be made, and the overall attack rate and age-specific attack rate computed.
3. Active case detection shall be carried out among contacts in the institution and family, and all those with illness shall be referred for treatment at the nearest health clinics.
4. Where a case is observed or suspected to have unusual signs and symptoms e.g. seizures, weakness of limbs, profound lethargy, refusal to play, the case shall be immediately referred to hospital.
5. Swabs from oral ulcers and vesicular lesions on the hands and feet shall be collected for virus isolation at identified laboratories (IMR or NPHL). If these ulcers and vesicles are no longer present, stool specimens shall be sent. Always consult pathologist for specimens taking, handling and transportation.

6. Principals, teachers and supervisors shall be alerted to look out for children with fever, rash / blisters on palms and soles and to isolate them immediately. Screening before coming to class is recommended (please refer *Buku Panduan Latihan Taska dan Prasekolah*).
7. Health education of supervisors of institutions on the disease, mode of transmission, importance of good personal hygiene and isolation of infected children shall be carried out.
8. Close the premise closed for two incubation period (10 days) from the date of onset of the last case. Supervision on disinfection procedures shall be given to the premise operators.

In addition the investigating team shall also look into environmental sanitation and hygiene to ensure that:

a. Articles such as toys contaminated by infected cases are disinfected with 0.5% sodium hypochlorite solutions (please refer *Buku Panduan Latihan Taska dan Prasekolah*).
b. A high standard of food and personal hygiene is maintained by the institution involved which include proper waste and diapers disposal.
c. The approved enrolment of Department of Social Welfare (JKM), Ministry of Education, Department of National Integration and other relevant parties, where applicable, and shall notify the relevant authorities if regulations not complied.

If the outbreak occurs in primary schools;

i. Ensure that the infected students remain away from the institution for at least ten days.
ii. Health education to the students on the disease, mode of transmission, importance of good personal hygiene.
iii. Principals, teachers and supervisors shall be look for children with fever, rash / blisters on palms and soles and to isolate them immediately. Screening before coming to class is recommended (please refer *Buku Panduan Latihan Taska dan Prasekolah*).
iv. If closure is necessary, just closed the affected class. Closure of the whole school is unnecessary as HFMD in older children is usually very mild and so far no complication has been documented from this agegroup.

6.5 Documentation and review

Disease activity and emergency response should be adequately documented so that further outbreaks can be handled more effectively. A summary report should be prepared within a month from the last date of case; and distributed to all the stakeholders for feedback. Format of report, dissemination and tabling of report is discussed in more details in Infectious Disease Outbreak Rapid Response Manual.[12]

Appendix 1

Variables required in HFMD surveillance database

1 Epid week
2 Name
3 Age
4 Sex
5 Ethnic
6 Home address
7 Locality
8 District
9 Name of school / preschool / nursery
10 Address of school / preschool / nursery
11 Date of onset
12 Case definition fulfilled
13 Symptoms and signs of CNS
14 Contact with HFMD case
15 Address of contact
16 Date of seen
17 Name of clinic / hospital
18 Government or private health facility
19 Outpatient or inpatient treatment
20 Date of admitted
21 Date of discharge
22 Date of death

Appendix 2(i)

No. Rujukan Makmal	

NATIONAL ENTEROVIRUS SURVEILLANCE
DIAGNOSTIC REQUEST FORM

A. MAKLUMAT PESAKIT		
Negeri :	Daerah :	
Hospital (wad) / Klinik Kesihatan		No. R/N :
Nama Pesakit :		
No. K/P :	Umur :	Jantina : L / P
Bangsa :	Tarikh lahir :	

B. MAKLUMAT KLINIKAL		
Gejala (Simptom)	Ada / Tiada (Tandakan √)	Tarikh mula
Demam > 38 ^{0}C		
Ulser di mulut & tekak		
Maculopapular rashes dan / Vesikel pada tapak tangan dan tapak kaki		
Tanda dan gejala URTI		

C. SPESIMEN KLINIKAL			
Spesimen		**Tarikh diambil**	**Tarikh penghantaran**
Rectal swab		/ /	/ /
Mouth ulcer		/ /	/ /
Vesicle swab		/ /	/ /
Stool		/ /	/ /

D. MAKLUMAT PEMOHON	
Nama dan Cop Pegawai : Tandatangan :	No. telefon : No. fax : e-mail :

E. MAKMAL (Untuk Kegunaan Makmal)			
Keadaan spesimen :			Tarikh terima spesimen :
Spesimen	**Jenis ujian**	**Keputusan ujian**	**Komen**
Rectal swab			
Mouth ulcer			
Vesicle swab			
Stool			

Nama dan tandatangan Pegawai Makmal :	
Jawatan Pegawai Makmal dan Cop Makmal :	Tarikh :

Nota * : All samples except blood / serum and stool must be in the viral transport media (VTM) and send immediately in ice pack to HUKM Microbiological Laboratory.

Appendix 2(ii)

Variables Required for Enterovirus Surveillance Database

Name of Centre / Laboratory: _____

No	Date Sample Received	Date Sample Collected	LN	RN	Name	Ethnic	Age	Sex	Source	Case diagnosis	Type of spec	Result		
												IF	Isolation	PCR

BORANG SIASATAN PESAKIT DI WAD
PENYAKIT TANGAN, KAKI DAN MULUT (HFMD)
BAHAGIAN KAWALAN PENYAKIT, KEMENTERIAN KESIHATAN MALAYSIA

BAHAGIAN 1

Tarikh masuk wad: ☐☐☐☐☐☐ Masa: ☐☐☐☐

Tarikh discaj: ☐☐☐☐☐☐ Masa: ☐☐☐☐

Tarikh kematian ☐☐☐☐☐☐ Masa: ☐☐☐☐

A. PERIHAL PESAKIT

1. Nama pesakit:
2. Tarikh lahir: ☐☐☐☐☐☐
3. Nama ibu:
4. No K/P ibu:
5. Alamat rumah:
6. No telefon: (rumah)
(H/P)

Kedudukan rumah (GPS): X : _____ Y : _____

7. Jantina: ☐ Lelaki ☐ Perempuan

8. Kumpulan etnik
☐ Melayu ☐ Kadazan/Dusun
☐ Cina ☐ Murut
☐ India ☐ Bajau
☐ Asli semenanjung ☐ Melanau
☐ Bidayuh ☐ Iban
☐ Lain-lain pribumi ☐ Lain-lain (nyatakan) Sabah/ Sarawak

9. Kewarganegaraan: ☐ Malaysia ☐ Warga asing

10. Menghadiri sekolah / taska
☐ Ya
☐ Taska / Nurseri
☐ Prasekolah
☐ Sekolah
Nyatakan nama: _____
☐ Tidak

B. MAKLUMAT KLINIKAL

1. Tarikh mula sakit (onset) ☐☐☐☐☐☐☐☐

2. Tanda dan gejala: Ya Tidak
Riwayat demam ☐ ☐

Ulser mulut	☐	☐
Ruam (rash) tapak tangan / kaki	☐	☐
vesicles di tapak tangan / kaki	☐	☐

3. Kompliksi	Ya	Tidak
Aseptic meningitis	☐	☐
Myocarditis	☐	☐
Encephalitis	☐	☐
Acute flaccid paralysis	☐	☐
Jika ya, sila nyatakan bahagian anggota: _____		
Kematian	☐	☐

C. MAKLUMAT UJIAN MAKMAL

SAMPEL	Tarikh diambil	Keputusan	Tarikh keputusan
Throat swab			
Rectal swab			
Vesicle swab			
Stool			
Blood			
CSF			
Biopsy _____ (Nyatakan tisu)			

D. MAKLUMAT PEGAWAI YANG MERAWAT

1. Nama Pakar / Pegawai Perubatan: _____ Tandatangan: _____
2. Nama Wad: _____
3. Nama hospital: _____ Tarikh notifikasi: _____

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