KEY FEATURES OF EV71 INFECTION AT A GLANCE (Version 2.03) 27 May 08

1. THE DISEASE

80% cases result in HFMD which is a self-limiting disease in the majority of affected patients, usually children. It may also cause herpangina or undifferentiated fever.

2. SEVERE DISEASE MANIFESTATIONS

It may occur in previously healthy or immunocompetent subjects, which include:

- Aseptic meningitis
- Encephalitis (eg brainstem encephalitis or rhombencephalitis)
- Encephalomyelitis
- Acute flaccid paralysis (typically monoplegia)

3. WHEN TO SUSPECT

Patients presenting with fever, papulovesicular rash involving the distal extremities, buttocks and extensor surfaces of the knees, and oropharyngeal ulcers. The importance of eliciting a contact history cannot be over-emphasized. The classical clinical features of HFMD are not necessarily always present together.

4. LAB DIAGNOSIS

Specimens should be taken in the early phase of the disease:

- Faeces (shedding continues for a few weeks) for RT-PCR and viral isolation
- Nasopharyngeal aspirate or throat swab (within the first few days of onset of illness) for RT-PCR and viral isolation
- Others - vesicle fluid, CSF and tissue for RT-PCR and virus isolation
- Paired serum samples for serology

5. WARNING SIGNS OF SEVERE ILLNESS

- Persistent sleepiness / drowsiness,
- Repeated vomiting,
- Frequent myoclonic jerks (e.g. several times / hour).

6. WHEN TO CONSIDER ADMISSION

Children (especially < = 5 years of age) with HFMD / herpangina, or who are close contacts of known cases of HFMD / herpangina, should be considered for hospitalization if the following warning signs are detected within 7 days of onset of illness:

- High fever (> 39^{0}C)
- Persistent fever (> 3 days)
- Neurological features
  - Irritability, sleepiness, frequent sleep interruption, drowsiness, difficulty to arouse, fluctuating consciousness, hallucinations, vision problem (diplopia, photophobia), persistent headache, repeated vomiting, bulging anterior fontanelle in infants, neck pain or neck stiffness, abnormal posture or tone, myoclonic jerks, ataxia, limb weakness, abnormal eye movements, cranial nerve palsy
- Autonomic disturbance (increased sympathetic tone)
  - increased startle reflex, insomnia, panic attacks, pallor, cold sweating, tremor, abdominal distension (paralytic ileus), urinary retention (atonic neurogenic bladder), hypertension,,tachycardia, hyperglycaemia, leucocytosis
- Cardiopulmonary features: pallor, cyanosis, tachypnoea, hypotension, tachycardia, bradycardia, arrhythmia, poor peripheral circulation
- Others
  - Poor feeding, decreased urine output

7. PATIENT MANAGEMENT

- Supportive and symptomatic treatment.
- Early detection of signs of CNS involvement (especially brainstem), careful monitoring of fluid balance, and accurate assessment of left ventricular function
- HR, RR, BP, SpO2 for cardiopulmonary decompensation.
- Early intubation with mechanical ventilation and prompt institution of neurointensive care if conscious level deteriorates or cardiopulmonary collapse (progression to severe cerebral oedema and fulminant pulmonary edema +/- pulmonary haemorrhage)
- Specific antiviral therapy is not available.
- ICU admission for signs of organ failure
- Consult Paediatric ID specialist for need for IVIG therapy

8. INFECTION CONTROL

- Affected children should not attend schools or day care
- Standard Precautions should be strictly observed in healthcare settings. Hand hygiene is of utmost importance.
- Contact Precautions for duration of illness are indicated for infants and young children or if the patient is incontinent and may contaminate the environment and for control of institutional outbreaks.
- Restrict the direct contact of patients suffering from HFMD/enterovirus infection with other patients.
- Place / cohort the patient in an isolation room as far as possible .
- Use of one part of 5.25% hypochlorite solution added into 49 parts of water would be sufficient for disinfection.
- Linen and waste from patients suffering from HFMD should be handled with care, and wash hands after handling.

9. REPORTING OF CASES

- Inform the hospital's Infection Control Team of cases of HFMD or herpangina admitted for severe complications .
- Suspected clusters of HFMD or confirmed cases of EV71 should be reported to the CENO of CHP

For full details, please refer to the HA-IDC, CHP ICB and CCID-ER Fact sheet on Enteroviral Infection for Hospital (Apr 2008 version 2.03) accessible on ha.home.

1. Title

Fact Sheet on Enteroviral Infection for Hospitals

2. Causative Agents

- Enteroviruses (EV) refer to a group of small, non-enveloped RNA viruses comprised of four species, namely Polioviruses (3 serotypes), Coxsackieviruses (group A: 23 serotypes, group B: 6 serotypes), Echoviruses (31 serotypes) and Enteroviruses (4 serotypes, namely type 68-71).
- The commonest cause for Hand, Foot and Mouth Disease (HFMD) is Coxsackievirus A16. Other types of enteroviruses have also been associated with this syndrome, such as Coxsackieviruses A4, A5, A9, A10, B2, B5 and EV 71.
- Compared to other enteroviruses, EV71 is more often associated with severe complications such as encephalitis and poliomyelitis-like paralysis
- EV can survive for days on fomites at room temperature.
- Inactivation at temperatures above 60ºC

3. Epidemiology (refer to appendix 1 for the annual number of enterovirus isolates detected)

- EV are spread by the following routes, namely, faecal-oral, respiratory droplets, and direct contact with objects (e.g. toys or appliances) contaminated by faeces or respiratory secretions/vesicular fluids from infected persons. Infants in diapers appear to be the most efficient transmitter.
- The incubation period for Hand-foot-and-mouth Disease (HFMD) is 3 to 7 days.
- Enteroviral infections peak in May to July.
- Young children are its main target and reservoir but adults can also be infected.
- The infectious period starts from several days before the appearance of symptoms and peaks within one week of disease onset. The virus may be excreted in the stools for 6-8 weeks and in respiratory secretion for 1 week.
- HFMD caused by EV71 infection may be complicated by encephalitis or poliomyelitis-like paralysis. From 2005-2007, 36 cases of EV-71 infections were reported. Up till 24 May 2008, 33 cases of EV-71 infection were notified to CHP.

4. Clinical Manifestations

- Enteroviral infections are mostly subclinical or presented as non-specific febrile illness.
- The same virus can cause several different clinical syndromes. Conversely, the same clinical picture can be caused by different enteroviruses.

Syndrome/Disease	Predominant virus	Clinical features
Nonspecific febrile illness	All types	Fever with upper respiratory and/or gastrointestinal symptoms
Meningoencephalitis	Echoviruses, Enterovirus 71, Coxsackieviruses A & B	Fever, meningeal signs, change in mental status, seizure
Herpangina	Coxsackieviruses A & B	Fever, painful oral vesicles and/or ulcers on tonsils and posterior pharynx

Hand, foot and mouth disease	Coxsackievirus A16, A9 Enterovirus 71	Fever, vesicles and/or ulcers on buccal mucosa and tongue and on interdigital surfaces of hands and feet
Non specific exanthem	Echoviruses	Variable rash +/- fever
Myocarditis/pericarditis	Coxsackieviruses B	Uncommon, myocarditis/pericarditis may present as heart failure or dysrhythmia
Acute haemorrhagic conjunctivitis	Enterovirus 70 Coxsackieviruses A (Adenoviruses)	Epidemic cause of conjunctivitis with lid swelling, subconjunctival haemorrhage and eye pain without systemic symptoms
Neonatal disease	Coxsackieviruses B Echoviruses	Sepsis like picture, meningo-encepahalitis, hepatitis, myocarditis
Pleurodynia	Coxsackievirus B3, B5	Uncommon, epidemic, fever and severe muscle pain of chest and abdomen
Acute flaccid paralysis	Coxsackievirus A7, Echoviruses, Enterovirus 71	Fever followed by sudden asymmetric flaccid paralysis

- Enteroviruses are probably the commonest cause of aseptic meningitis.
- **Special Features of Enterovirus 71 (EV71):**

  - 80% cases result in HFMD which is a self-limiting disease in the majority of affected patients, usually children.

  - Epidemic HFMD may also be caused by Coxsackievirus A9 and A16. It is not uncommon to see both EV71 and Coxsackievirus A16 co-circulating during an epidemic of HFMD.

  - EV71 may also cause herpangina or non-specific febrile illness (undifferentiated fever).

  - EV71 can occasionally cause severe diseases even in previously healthy or immunocompetent subjects, which include:

    ✓ Aseptic meningitis
    ✓ Encephalitis (in particular, brainstem encephalitis or rhombencephalitis)
    ✓ Encephalomyelitis
    ✓ Acute flaccid paralysis (typically monoplegia)

  - Fatalities from severe EV71 infection have been recorded especially in young children during previous epidemics occurring both locally and abroad (Malaysia, Singapore, Taiwan etc.).

  - High index of suspicion needed: EV71 infection should be suspected in patients presenting with fever, papulovesicular rash involving the distal extremities, buttocks and extensor surfaces of the knees, and oropharyngeal ulcers. The importance of eliciting a contact history cannot be over-emphasized. The classical clinical features of HFMD, however, are not necessarily always present together, even in patients with severe EV71 infection. The combination of presenting features can be variable. Scanty papular skin rash without vesicular eruption, absent or minimal oropharyngeal

ulcers, absence of fever or just fever without cutaneous or mucosal lesions at presentation have all been documented, even in fatal cases.

HFMD with full-blown clinical features are difficult to miss, but delayed diagnosis and hence appropriate management of severe EV71 infection in the absence of complete presenting signs and symptoms of HFMD will be inevitable if a high index of suspicion is not consistently maintained during an epidemic of HFMD, with serious consequences.

5. Laboratory Diagnosis

Viral studies for enteroviruses should focus on hospitalised patients with any of the following conditions:

- HFMD/Herpangina/suspected enterovirus infection* with rapid clinical deterioration or complications like
  - aseptic meningitis / encephalitis;
  - acute flaccid paralysis;
  - pulmonary edema/pulmonary hemorrhage/ARDS
  - myocarditis.

* Rash or oral lesions may not be present

Specimens should be taken in the early phase of the disease, including;

- faeces (shedding continues for a few weeks);
- nasopharyngeal aspirate or throat swab (within the first few days of onset of illness);
- others as appropriate - vesicle fluid, CSF, eye swab and tissue.

Specimens, except CSF, should be put in viral transport medium (T/M) and kept at 4^0 C during transport to the laboratory. RT-PCR and culture can be performed on the same specimen.

i) RT-PCR is indicated for patients with suspected enteroviral infection complications as listed above.

a) Specimens can be sent with no prior arrangement but with clear specification of `HFMD complications' and request for EV-71 RT-PCR to one of the following laboratories:

- Virology Division, PHLC, CHP
- Virology Laboratory, Department of Microbiology, QMH

b) Turnaround time: 1-2 days (if the specimens arrive at the respective laboratories before noon on day 1, results will be available before 5 pm the following working day).

ii) Viral isolation can be performed on specimens from all patients suspected of enterovirus infection although this is of variable sensitivity.

a) Specimens should be sent to the Government Virus Unit, PHLC or Virology Laboratory of QMH, following existing arrangement.

b) Turnaround time: Up to 7 -8 days for final viral identification. (This may have

infection control significance: clinicians might advise patients not return to nursery or school after discharge until the investigation result is known to be negative for EV-71, since the current CHP recommendation is to avoid returning to school for 2 additional weeks after the symptoms subside)

iii) Serologic testing is also available at QMH for retrospective diagnosis of unusual cases. Paired serum samples (acute and convalescent) should be taken at least 14 days apart. Please call Dr. KH Chan (2855-4194) to arrange

* Notes on diagnostic methods based on specimen types:

- RT-PCR has superior sensitivity compared to cell culture for the identification of enteroviruses in the CSF (up to 86 percent versus 30 percent).
- Among patients with CNS manifestations and a negative CSF PCR, upper respiratory tract and gastrointestinal tract specimens for enterovirus PCR may be needed to establish a diagnosis of enterovirus infection.
- Sensitivity of PCR compares favorably to that of culture for respiratory and serum specimens, although urine culture may still be superior to urine PCR. Limitations to PCR include availability and serotyping capabilities.
- Because the EVs are shed from the oropharynx and gastrointestinal (GI) tract for weeks to months after infection, their detection from these sites must be cautiously interpreted. Their presence at these sites does not establish causality of the syndrome being evaluated.
- The identification of an EV from the CSF, blood, tissue or urine (if sterilely obtained), is strongly supportive of an invasive infection and carries with it a high probability of being the causal agent of the patient's illness. Samples from these sites represent the ideal sources from which to diagnose EV infections

6. Patient Management

6.1 For out-patients

Most cases of HFMD and herpangina are mild and do not warrant hospitalization. Only symptomatic treatment and attention to adequate hydration are required.

Affected children should not attend schools or day care

Children (especially < = 5 years of age) with HFMD / herpangina, or who are close contacts of known cases of HFMD / herpangina, should be considered for hospitalization if the following warning signs are detected within 7 days of onset of illness:

- High fever (>39^{0}C)
- Persistent fever (>3 days)
- Neurological features
  - irritability, sleepiness, frequent sleep interruption, drowsiness, difficulty to arouse, fluctuating consciousness, visual or auditory hallucinations, diplopia, photophobia, persistent headache, repeated vomiting, bulging anterior fontanelle in infants, neck pain or neck stiffness, abnormal posturing, generalized hypotonia or rigidity, myoclonic jerks, unsteady gait, ataxia, limb weakness, abnormal eye movements (sustained upward gaze, nystagmus, opsoclonus), squint, cranial nerve palsy

- Autonomic disturbance (increased sympathetic tone)
  - agitation, insomnia, increased startle reflex, panic attacks, pallor, cold sweating, tremor, tachycardia out of proportion to the degree of fever, hypertension, abdominal distension (paralytic ileus), urinary retention (atonic neurogenic bladder), hyperglycaemia, leukocytosis
- Cardiopulmonary features
  - pallor, cyanosis, tachypnoea, shortness of breath, hypotension, cold extremities, poor peripheral circulation, delayed capillary refill, tachycardia, bradycardia, irregular pulse rhythm
- Others
  - poor feeding, decreased urine output

Based on the clinical experience in Taiwanese children, the 3 most important warning signs of severe EV71 infections appear to be:

- persistent sleepiness / drowsiness,
- repeated vomiting,
- frequent myoclonic jerks (e.g. occurring several times or more in an hour).

If patients are fit for discharge from A&E Department or GOPD, advice on seeking early, if not immediate, medical attention should be given if the above warning signs are observed. For example, a statement as shown below can be given:

" Your child has been diagnosed to have hand, foot and mouth disease. This disease is normally not dangerous but 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 irritability
- repeated jerky limb movement

6.2 For in-patients

- Prompt recognition of clinical deterioration and supportive treatment is the mainstay of management.
- Secondary cases from household contact may be more severe (inoculum effect or initial high viral load due to prolonged close contact) and require closer observation.
- Early detection of signs of CNS involvement (especially brainstem), careful monitoring of fluid balance, and accurate assessment of left ventricular function are of critical importance.
- Patients should be closely monitored (HR, RR, BP, SpO2) for cardiopulmonary decompensation.
- Lumbar puncture for CSF examination can be deferred (to be performed later when clinical condition is stabilized) in the following situations:
  - rapidly deteriorating conscious level
  - status epilepticus

- unstable cardiorespiratory status
- evidence of significantly raised intracranial pressure
- presence of focal neurological signs

- Neuroimaging with CT or MRI is indicated in case of persistent or progressive neurological signs with or without accompanying cardiopulmonary collapse or pulmonary oedema.
- When deterioration of consciousness is noted, early intubation with mechanical ventilation, and prompt institution of neurointensive care are desirable since the patient may rapidly progress to severe cerebral oedema and fulminant pulmonary edema +/- pulmonary haemorrhage.
- The pulmonary oedema is believed to be neurogenic in origin and not due to myocarditis. It is postulated that autonomic dysregulation as a result of brainstem encephalitis leads to increased catecholamine release which causes intense generalised vasoconstriction (an initial phase of hypertension may be noted), high systemic vascular resistance and increased afterload to the heart culminating in left ventricular failure, passive pulmonary volume overload and catastrophic pulmonary oedema or pulmonary haemorrhage. The role of immunopathologic mechanisms (e.g. hypercytokinemia or cytokine storm triggered by overwhelming viral sepsis) in the pathogenesis of pulmonary oedema has also been suggested.
- Based on one Taiwanese case series, the risk factors for the development of neurogenic pulmonary oedema include hyperglycaemia, leukocytosis and limb weakness.
- Consider left ventricular failure and perform early echocardiographic assessment if apparent shock or cardiovascular collapse fails to respond to initial fluid resuscitation (e.g. hypotension not corrected after 2-3 bolus infusions of 20 ml/kg of volume expanders in children). Appropriate inotropic support should be instituted when indicated.
- Vigorous fluid resuscitation with volume overload may be detrimental by aggravating the established or impending pulmonary oedema if the condition is not suspected.
- Specific antiviral therapy is not available.
- The efficacy of intravenous immunoglobulin (IVIG) therapy in severe EV71 infection remains to be proven. The Centre for Disease Control of Taiwan does not recommend its use in children >5 years of age.
- The indications for IVIG therapy proposed by Taiwan CDC include:
- (1) children with HFMD / herpangina

or

(2) children who are close contacts of confirmed HFMD / herpangina cases (i.e. only an epidemiologic link in the absence of clinical features of either condition)

and

who develop the following signs during the course of illness:

- myoclonic jerks plus unexplained tachycardia (HR >150/min)
- acute flaccid paralysis
- acute encephalitis, especially if accompanied by specific features of focal brainstem dysfunction such as ataxia, cross hemiplegia, cranial nerve palsy or brainstem dysautonomia

- acute respiratory failure (acute pulmonary oedema, pulmonary haemorrhage, ARDS)
- heart failure
- sepsis syndrome (not recommended if complicated by multiorgan failure)

- When IVIG is considered, the regimen recommended by Taiwan CDC is 1 g/kg infused over 12 hours for once only.

7. Infection Control Measures

- Standard Precautions should be strictly observed in healthcare settings. Hand hygiene is of utmost importance. Contact Precautions for duration of illness are indicated for infants and young children or if the patient is incontinent and may contaminate the environment and for control of institutional outbreaks.
- Health care workers should;
  a. Observe hand hygiene practice immediately and thoroughly after handling patients secretions or excretions irrespective of whether or not gloves are worn. Wash hands if there is visible soiling on hands;
  b. Wear gloves and gown during patient-care activities that are likely to involve contact with patient's secretions or excretions; Remove the gloves and gown upon leaving the patient environment
  c. Put on personal protection equipments e.g. mask, faceshield when carrying out procedure that is likely to generate splashes to mucous membranes.
- Place /cohort the patient in an isolation room as far as possible ; No negative pressure needed for isolation room.
- Restrict the direct contact of patients suffering from HFMD/enterovirus infection with other patients.
- Disinfect the patient items properly. Use of one part of 5.25% hypochlorite solution added into 49 parts of water would be sufficient for such purpose.
- Linen and waste from patients suffering from HFMD should be handled with care, and wash hands after handling.
- Advice to the patients or parents/ caretakers: Pay attention to hand hygiene cleanliness. Do not let children attend nurseries/kindergartens/schools/activities that mix with other children until afebrile and all vesicles have dried up (If enterovirus-71 is confirmed to be the pathogen, then take 2 more weeks of sick leave after all vesicles dry up) ; or to follow the advice from CHP if there is an outbreak

8. Reporting of Cases

A. Staff of AED and Paediatrics Dept

- Inform the hospital's Infection Control Team of critical or fatal cases admitted for severe complications like meningitis/encephalitis, acute flaccid paralysis (AFP), myocarditis.
- When EV-71 is confirmed, report to hospital ICT, CENO following the reporting procedures specified under HA Guideline using the Clinical Record Form.

B. Infection Control Team

- Inform CICO, Hospital administration and CENO. It is important to ask for any contact history of patient with HFMD or cluster of persons with fever and rash. Suspected clusters of HFMD or confirmed cases of EV71 should be reported to the CENO of CHP

9. Reference and further sources of information:

A. Alexander JP Jr, Baden L, Pallansch MA, Anderson LJ. Enterovirus 71 infection and neurologic disease—United States, 1977–1991. J Infect Dis 1994;169:905–8.

B. Sawyer MH, Holland D, Aintablian N, Connor JD et al . Diagnosis of enteroviral central nervous system infection by polymerase chain reaction during a large community outbreak Pediatr Infect Dis J 1994;13(3):177-82.

C. Rotbart HA, Ahmed A, Hickey S, Dagan R et al. Diagnosis of enterovirus infection by polymerase chain reaction of multiple specimen types. Pediatr Infect Dis J 1997;16(4):409-11.

D. Chang LY, Huang YC, Lin TY. Fulminant neurogenic pulmonary oedema with HFMD. Lancet 1998;352:367.

E. The Centers for Disease Control and Prevention. MORBIDITY AND MORTALITY WEEKLY REPORT MMWR 1998;47(30):629-632.

F. Chang LY, Lin TY, Hsu KH, Huang YC et al. Clinical features and risk factors of pulmonary oedema after enterovirus-71-related hand, foot, and mouth disease Lancet 1999;354:1682–86

G. Huang CC, Liu CC, Chang YC, Chen CY et al. Neurologic Complications in Children with Enterovirus 71 Infection. N Engl J Med 1999;341:936-942

H. Ho M, Chen ER, Hsu KH, Twu SJ et al. An Epidemic of Enterovirus 71 Infection in Taiwan. N Engl J Med 1999;341:929-935

I. AbuBakar S, Chan YF, Lam SK et al. Outbreaks of Enterovirus 71 Infection. N Engl J Med 2000;342:355-356

J. Centre for Disease Control, Taiwan accessible at http://203.65.72.83/En/dqia/ShowPublication.ASP?RecNo=931

K. Nolte FS. Case studies in cost effectiveness of molecular diagnostics for infectious diseases: pulmonary tuberculosis, enteroviral meningitis, and BK virus nephropathy Clin Infect Dis. 2006 1;43(11):1463-7.

L. Pérez-Vélez CM, Anderson MS, Robinson CC et al. Outbreak of neurologic enterovirus type 71

disease: a diagnostic challenge Clin Infect Dis. 2007 15;45(8):950-7.

M. Scientific Committee on Enteric Infections and Foodborne Diseases. Strategies for the Prevention and Control of EV 71 Infection in Hong Kong: http://www.chp.gov.hk/files/pdf/sas4_ev71_20050927.pdf

N. Centre for Health Protection . Letters to Doctors. Guideline on Hand-foot-mouth Disease (HFMD) Management in health care settings issued on 23 May 2007. accessible at http://www.chp.gov.hk/files/pdf/letters_to_doctors_2007052301.pdf

O. Department of Health, Hong Kong. Statistics on on Communicable Disease : Hand, foot and mouth disease. Yearly Enteroviral infections from 1994-2008(Jan-Feb) http://www.chp.gov.hk/data.asp?lang=en&cat=4&dns_sumID=53&id=292&pid=44&pd=26

P. Taiwan CDC. Guidelines on clinical management of enterovirus infection and its complications (in Chinese) . Accessible at http://www.cdc.gov.tw/pubic/Attachment/831713474771.pdf

Q. Taiwan CDC. Guidelines on clinical management of severe cases of EV71 infection in health care settings. (in Chinese) Accessible at http://www.cdc.gov.tw/public/Attachment/811410151271.pdf

R. US CDC. Guideline for Isolation Precautions: Preventing Transmission of Infectious Agents in Healthcare Settings 2007. Accessible at http://www.cdc.gov/ncidod/dhqp/gl_isolation.html

S. Centre for Health Protection. Guidelines on prevention of communicable diseases in child care centres / kindergartens / schools.
Accessible at http://www.chp.gov.hk/files/pdf/Guild-Booklet-eng.pdf

Appendix 1: Yearly Enterovirus infections 1994 - 2008 (Jan-Feb)

(Source: Centre for Health Protection, Department of Health, Hong Kong http://www.chp.gov.hk/data.asp?lang=en&cat=4&dns_sumID=53&id=292&pid=44&ppid=26)

Year	No. of infections			
	Coxsackieviruses	EV71	Other Enteroviruses	Total
1994	111	0	22	133
1995	36	1	34	71
1996	49	0	21	70
1997	30	2	32	64
1998	170	60	332	562
1999	214	22	111	347
2000	269	6	83	358
2001	230	30	24	284
2002	459	5	13	477
2003	46	1	6	53
2004	226	35	21	282
2005	415	8	79	502
2006	428	21	82	531
2007	286	12	24	322
2008 (Jan-May)	17	22 (as of May 19)	pending	pending