



Figure 5. Comparison of HFMD critical case prior (left) and after (right) medical treatment was provided at Fuyang No.2 hospital.

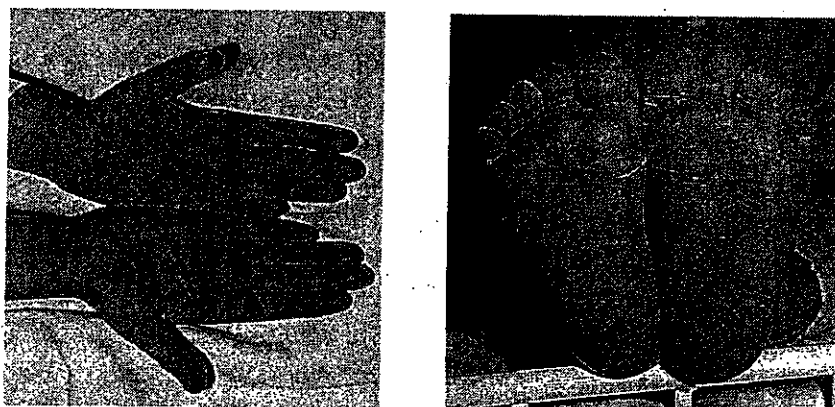


Figure 6. The rash of HFMD cases (on hand and foot)

## B. Descriptive analysis of the initial fatal cases

### 1) Epidemiological data

As of May 9, there have been 8 consecutive days without any fatalities reported by Fuyang City (See Figure 7). For the 22 fatal cases reported to date in Fuyang City, the gender distribution was 1:1, and age ranged between 3 months and 3 years. The number of fatal cases in age groups 0-, 1-, 2-, 3- was 6, 8, 7, 1, which accounted for 28%, 36%, 31% and 5% of cases, respectively. Fatal cases were reported in 5 districts and counties: Yinzhou (9, 41%), Yingquan (6, 27%), Funan (4, 18%), Linquan (2, 9%) and Yindong (1, 5%). The majority of fatal cases occurred in rural areas. Figure 5 shows the distribution over time according to date of onset of the fatal cases reported in Fuyang City between March 23 to April 29.

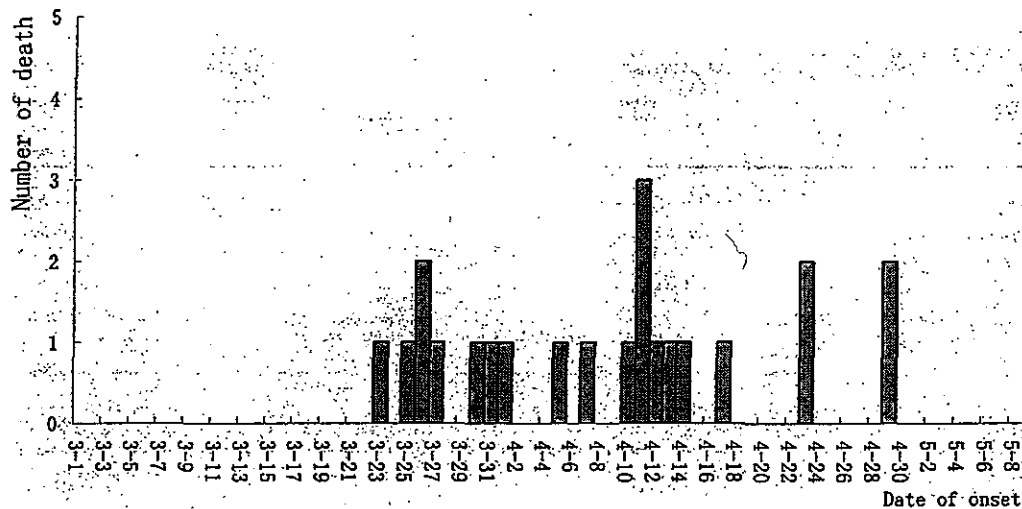


Figure 7. Fatal cases (n=22) by date of onset from March 23 to April 29 in Fuyang City.

### 2) Clinical symptoms

Data from 15 out of 22 fatal cases were analyzed. All cases were infants and had an acute onset of fever and influenza-like illness without catarrhal syndrome. Following general treatment guidelines for infectious respiratory diseases, local village or private doctors treated the patients with antibiotics without visible results. The condition of the cases deteriorated, developing tachypnea, cyanosis, and some presented seizures with foaming at the mouth of white or pink color. (See Table 3). Most hospitalized cases were preliminary diagnosed as severe pneumonia. Despite proactive medical procedures taken, the severe cases deteriorated rapidly and died. The mean duration between onset of symptoms and the hospitalization was 2 days; between hospitalization and time of death, 10 hours; and between onset of symptoms and time of death, 3 days. Further information on clinical conditions of the patients and their treatment will be discussed in an upcoming report.

Table 3. Clinical symptoms of fatal HFMD cases in Fuyang No.2 hospital (n=15).

Clinical symptom	Number of cases	proportion%
Fever	15	100
Tachypnea	14	93.3
Oral cyanosis	12	80.0
Pink foaming at the mouth	9	60.0
Coughing	7	46.7
Vomiting	8	53.3
Myoclonic twitching	3	20.0
Rash on palm, sole	6	40.0
Nasal discharge	2	13.3
Stiff neck	2	13.3

### 3) Exposure information

Epidemiological investigation revealed no contact between the 22 fatal cases. All cases were infants who had remained at home during the 2 weeks before the onset of symptoms. One case had been vaccinated within 1 month prior to onset of symptoms. Environmental investigation of the cases' households showed poor hygienic and sanitary conditions. All affected families had their own water well and none reported abnormalities after food consumption. In addition, no livestock die-off was reported by the affected families or in their village.

## **2. Laboratory testing and autopsy findings**

### **A. Laboratory testing of fatal cases**

Between March 31 and April 16, the Anhui CDC tested 53 specimens (including whole blood, blood serum, pharyngeal swab and tissue samples), collected from fatal HFMD cases, and tested negative for the presence of seasonal influenza, avian influenza A/H5N1, Severe Acute Respiratory Syndrome (SARS).

On April 18, the Institutes of Infectious Diseases and the Viral Diseases Prevention and Control of Chinese CDC received from Anhui CDC the previously collected specimens: pharyngeal swabs, lung puncture fluid, lung tissues, and blood. Laboratory testing for the presence of bacteria and virus was performed immediately on these samples. Specimens from 5 out of 12 fatal cases (42%) tested EV71 nucleic acid positive by RT-PCR. Of these 5 EV71 positive fatal cases, the lung tissue specimen tested EV71 positive for 1 case, and for another case, the intestinal lymph nodes, cerebrospinal fluid, spleen, thymus, kidney, brain, heart and lung specimens were EV71 positive. For the other 3 cases, the pharyngeal swabs were EV71 positive.

Viral isolation was conducted on 6 different types of specimens (including lung tissue, mouth efflux, brain tissue and pharyngeal swab) collected from 3 fatal cases. For all 6 specimens, the nucleotide sequencing and neutral antibody tests revealed the presence of EV71 virus.

### **B. Autopsy findings**

The autopsy on 3 fatal cases performed by the Medical School of Beijing University, found mainly changes in the brain, lung, heart and lymphatic system. There were cases of severe brain oedema; lung congestion/pulmonary oedema, no significant lung inflammation, no significant bleeding; cardiac enlargement; hypertrophy of tonsils, thymus and lymph nodes; spleen enlargement; normal kidney, liver and gastrointestinal organs. The autopsy findings were overall consistent with the clinical manifestations and disease progression and strongly suggest viral infection.

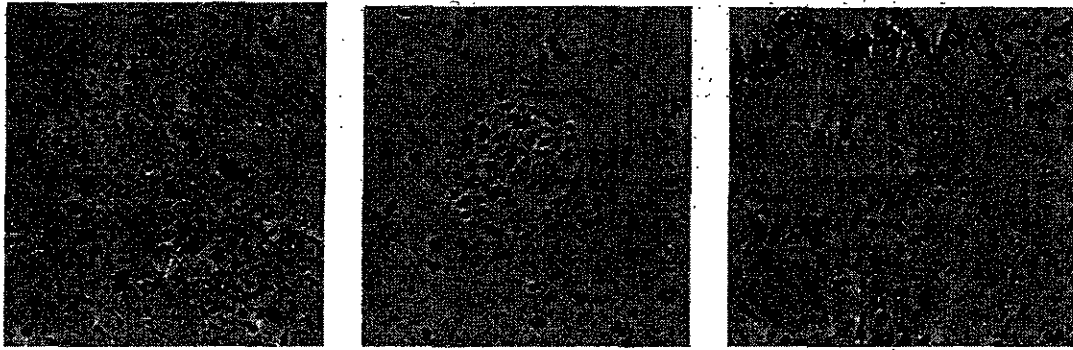


Figure 8. Left: brain tissue; Middle: spinal cord; Right: bronchus.

### C. Etiology study of mild HFMD cases

RT-PCR testing for EV71 was performed on 122 different Fuyang city specimens, including pharyngeal and rectal swabs, of which 61 (50%) were EV71 nucleic acid positive. Gene homogeneity was 99.3%-99.97% between the virus strains from mild cases (2 strains were from 2 mild cases) and fatal cases (6 strains were from 3 fatal cases). No neuro-virulence site mutation of the EV71 virus was found among severe and mild cases through bioinformatics analysis. Chinese CDC submitted the gene sequences of 3 virus strains to GenBank on May 7.

## Section 2 – Situation Analysis of HFMD in China

### I. Current HFMD situation in China

#### 1. HFMD surveillance

Before May 2, HFMD was not categorized as a notifiable disease and reporting of HFMD relied on voluntary reports submitted by clinicians. Since May 2, HFMD has been established as a class “C” notifiable disease, indicating that all clinical and laboratory diagnosed cases are reported through the web-based national disease surveillance and information management system. Standards for the clinical and laboratory diagnosis of HFMD cases can be viewed at the MOH website.<sup>2</sup>

#### 2. Occurrence of HFMD in China

From January 1 to May 9, 2008, 61,459 HFMD cases were reported through the disease reporting system in Mainland China. The incidence rate was 4.5/100,000, and the number

<sup>2</sup> Guideline for HFMD prevention and control, 2008 edition

<http://202.96.155.170/publicfiles/business/htmlfiles/mohjbyfkzj/s3577/200805/34775.htm>

of deaths reached 38 (case fatality rate 0.06%).

1) Time distribution

The number of reported cases has been increasing since April 28. After categorizing HFMD as a class “C” notifiable disease, reported cases increased sharply. For HFMD time distribution and date of reporting see Figure 9.

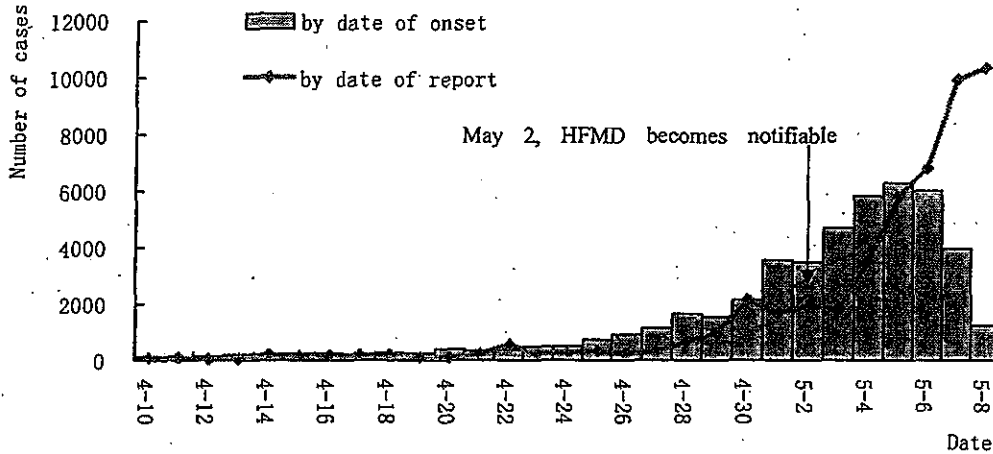


Figure 9. The number of HFMD cases by date of onset and date of reporting from April 10 to May 9, 2008 in China.

2) Geographical distribution

HFMD cases were reported in nearly all provinces in Mainland China. The 5 provinces with the highest number of reported cases are Guangdong (11,374), Anhui (9,235), Zhejiang (6,134), Shandong (4,566) and Henan (3,230).

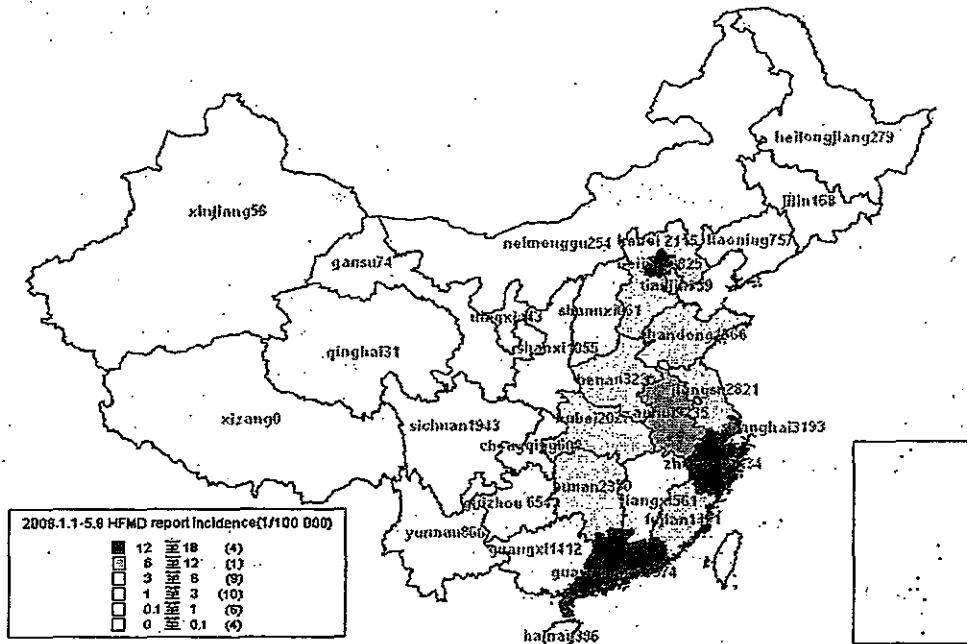


Figure 10 Incidence rate of HFMD cases by province in China from Jan 1 to May 9,2008

### 3) Age distribution

Children under 5 years old accounted for 92% of reported HFMD cases primarily affecting children ages 1 to 3 years old. See Figure 11 for the age distribution of HFMD in China.

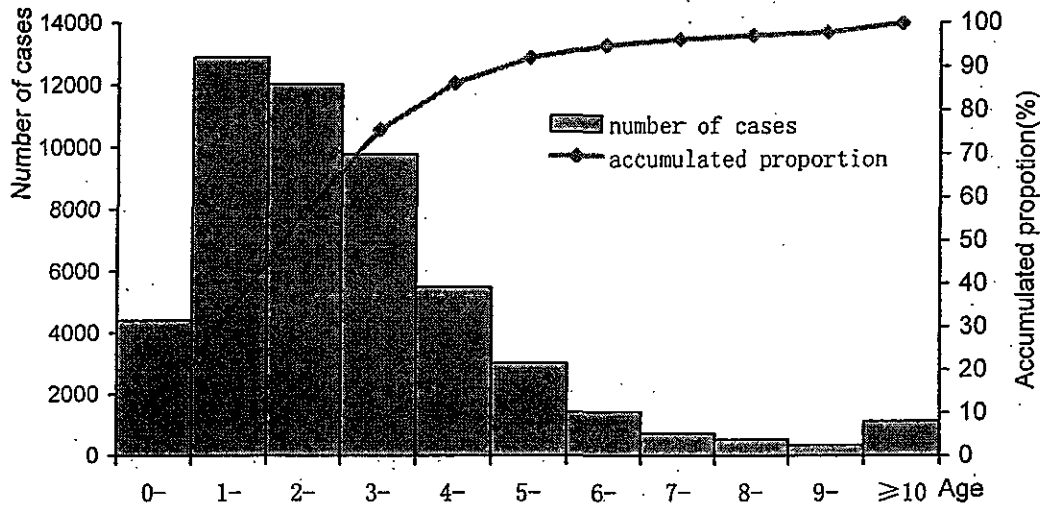


Figure 11. HFMD cases by age in China from January 1 to d May 9, 2008

### 3. Laboratory surveillance

After the identification of the HFMD outbreak in Fuyang City, Chinese CDC immediately began national-wide targeted laboratory testing on samples from HFMD cases. Up until May 9, 582 cases of samples from 23 provinces were tested positive for HFMD: EV71 accounted for 54.5%, Coxsackie A16 accounted for 17.4%, and other enteroviruses accounted for 28.2%.

## II. HFMD and EV71 infection in China before 2008

The first reported case of HFMD in Mainland China occurred in Shanghai in 1981. Since then, cases have been reported in Beijing, Hebei, Tianjin, Fujian, Jilin, Shandong, Hubei, Qinghai and Guangdong. In 1995, the Wuhan Virus Institute isolated the EV71 virus from HFMD patients. In 1998, Shenzhen CDC also isolated the EV71 virus from HFMD patients. There was a HFMD and Herpangina outbreak in Taiwan in 1998 with two outbreak waves occurring in June and October. 129,106 cases were reported from sentinel sites with a total of 405 severe cases and 78 deaths. The majority of cases were children under 5 years of age, and complications included encephalitis, aseptic meningitis, pulmonary oedema/pneumorrhagia, acute flaccid paralysis and myocarditis. In 2007, an HFMD outbreak occurred in Linyi City of Shandong Province with a total of 39,606 cases reported, including 14 deaths. Laboratory testing found the main etiologic pathogen to be EV71

while other detected enteroviruses were Echo3 and/or Coxsackie A16.

In 2007, there were 83,344 HFMD cases identified in Mainland China. The incidence rate was reported as 6.34/100,000 with a total of 17 deaths and case fatality rate of 0.02%. The majority of cases occurred in pre-school children (41% of all cases) or children in childcare centres (52%). Prevalence of HFMD in children under 10 years of age was high, accounting for 97% of total reported cases. The HFMD peak season is from May to October with most cases occurring between June and July (see figure 12). However, this may vary since HFMD was not a notifiable disease before 2008. Information on reported cases may be incomplete. Therefore, it is difficult to make an accurate estimation of past HFMD incidence in China.

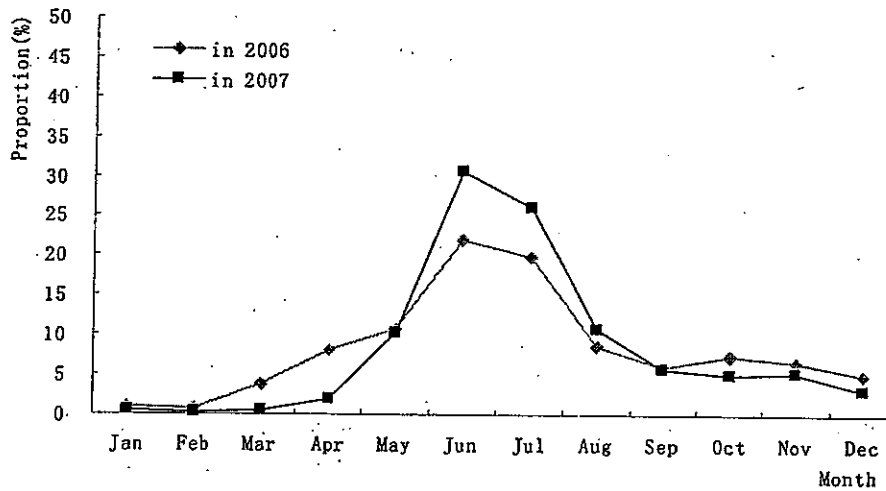


Figure 12 The distribution of HFMD cases by month in 2006 and 2007

## Section 3 – Outbreak Response in Fuyang City, Anhui Province and China

### I. The main response to the Fuyang City outbreak

#### 1. Strengthening of disease surveillance

A case definition was formulated for the early detection of severe cases and for the reporting, monitoring and treatment of severe cases.

A HFMD reporting protocol was developed, and daily reporting of HFMD is performed at each level of health care facility.