

## Risk of Transmission and Prevention Strategy Evaluation of Chikungunya Fever in Taiwan

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### Abstract

Recently, Chikungunya fever is continuously occurring in Southeast Asia where a popular travelling area is for Taiwanese people. To evaluate the risk of local transmission through importation and prevention strategy of this disease, we collected and analyzed disease data worldwide through literature review and Taiwan CDC Reporting System. Since Chikungunya fever was categorized as a notifiable disease in Taiwan from October, 2007, there were 26 imported cases by March, 2010. However, there was no local case noted in this time frame. The clinical signs include fever (65.4%), joint pain (11.5%) and cutaneous rash (19.2). The vectors of Chikungunya fever in Taiwan are *Aedes aegypti* (L.) and *Ae. albopictus* (Skuse), in which the later ones are distributed throughout entire Taiwan areas. Thus, large scale of epidemic of this disease may occur if there is no effective disease controlling measure when the pathogen invades. The main strategies for transmission prevention of this disease include: (1) Enhancing health education, (2) population warning, (3) improving medical diagnosis and treatment capability, (4) strengthen pathogen vectors

monitoring, (5) providing real time information, (6) establishing epidemic information, (7) controlling disease condition, (8) enhancing quarantine ability, and (9) preventing epidemics.

**Keywords:** chikungunya fever, infectious disease, risk evaluation

### Introduction

The pathogen of Chikungunya fever is chikungunya virus (CHIKV). The disease was first found in Africa in 1824. The virus was isolated from patient's serum samples in the Tanzania for the first time in 1953 [1]. Chikungunya in Makonde meant bending because some patients had swollen and painful joint and not able to move.

The clinical symptoms were similar to those of Dengue fever which including fever, headache, weary, nausea, vomit, joint pain and cutaneous rash. These symptoms may

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remain for few days to few weeks. This disease seldom causes death and, however, it induces extreme discomfort. Patients with severe symptoms may have joint pain and arthritis lasting for few weeks to few months, which severely impaired daily activity. This disease may be underestimated in epidemic areas of Dengue fever because of similar clinical signs [2].

Chikungunya fever is a viral disease transmitted by *Aedes*. Sub-Saharan Africa, tropical and subtropical zone in Asia and South America are epidemic areas. A large scale of Chikungunya fever epidemic was recorded in Tanzania, Eastern Africa, during 1952 to 1953 [1]. Between 1960 and 1982, there were several epidemics found in Africa and Asia [3]. Another large scale epidemic occurred in India in 2006, over 1.39 million cases were reported and more than 2,000 cases were confirmed. A smaller epidemic was found in Ravenna area in Italy, in which 200 cases were confirmed [4]. Recently, Chikungunya fever cases

were noted in Thailand, Malaysia, Singapore, Indonesia, India and Sri Lanka.

During these years, Chikungunya fever continuously occurs in Southeast Asian countries. People in Taiwan travelling to these areas become more frequently for tourism, visiting relatives and business. Chikungunya fever was included in the fever screening list at international airports since March, 2006. Furthermore, Taiwan CDC announced Chikungunya fever as a Category 2 notifiable disease in October, 2007, and all suspected cases should be reported to local health authorities and all necessary transmission preventive measures should be applied. This study discusses international situation of Chikungunya fever and evaluate the risk of invasion into Taiwan and response procedures for all epidemic prevention workers.

## Disease Information

### A. Pathogen

The pathogen of this disease is chikungunya virus (CHIKV, *Togaviridae*, *Alphavirus*). It was isolated for the first time from a serum sample of a Tanzanian patient in 1953 [5-6]. There are 3 main viral strains, including: 1) West African genotype: mainly distributed in Western Africa, 2) East/Central/South African genotype: mainly distributed in Western Africa, Central Africa, Eastern Africa, Europe, Australia and Eastern Asia, and 3) Asian genotype: mainly distributed in Southeast Asia [3, 7] (Figure 1). Virus particles can be detected from the saliva gland of *Aedes aegypti* (L.) and *Ae. albopictus* (Skuse) 2 days after mosquitoes sucking blood

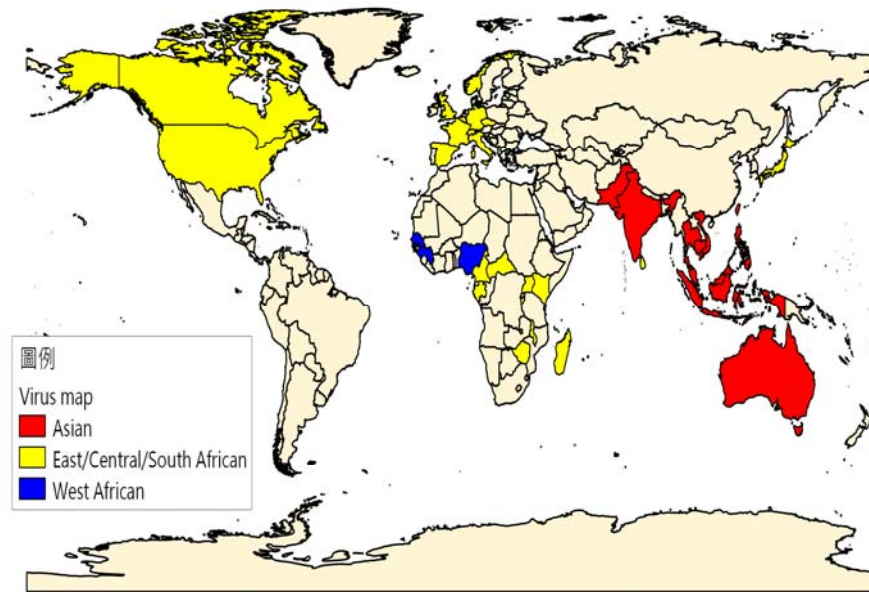


Figure 1. Geographic distribution of chikungunya virus [3, 7]

containing E1-A226V CHIKV. The viral concentration was higher in *Ae. albopictus* (Skuse) saliva gland than in those of *Aedes aegypti* (L.) The virus enters mid gut through blood and then crosses mid gut into body cavity. Viral replication occurs in body cavity and the virus infects saliva gland. Virus transmission between hosts is then proceeded through blood sucking [8]. The infection rate of chikungunya virus, as well as transmission rate, in *Ae. albopictus* (Skuse) is increased due to E1-A226V gene mutation, which also decreases the mid gut infection rate of *Aedes aegypti* (L.) [9-10].

### B. Transmission Vector

This disease is transmitted by *Aedes* sp. [11-12]. The species of vector mosquito is somehow different in various areas. In Asia, the pathogen is transmitted and maintained through urban cycle by *Ae. aegypti* (L.) and *Ae. albopictus* (Skuse) [13-14], while *Ae. furcifer* (Edwards) and *Ae. africanus* (Theobald) are the main

vectors with sylvatic cycle [15]. An epidemic was recorded in Reunion Island in 2005-2006 and *Ae. albopictus* (Skuse) was the vector [16]. In Taiwan, *Ae. aegypti* (L.) is mainly found in southern areas (Chia-Yi County and further southern), while *Ae. albopictus* (Skuse) is distributed throughout the entire Taiwan areas [17]. Beside vector transmission, some studies indicated that this disease can be spread out by blood transfusion, however, with lower risk [18]. Another report also showed evidence of vertical transmission of this disease. From 2006 to 2007 in Sri Lanka, 33 infected expectant mother procreated with viremia and 16 infants (48.5%) were infected by this disease. The transmission was suspected through placenta to fetus, but the mechanism was still unclear [19].

### C. Clinical Symptoms

Sudden fever, cold shiver, headache, myalgia, joint pain and cutaneous rash are main symptoms, which are similar (but with

different extent) to Dengue fever (Table 1). Symptom differences were noted comparing those cases in Taiwan (imported), India, Reunion Island and Malaysia (Table 2). Only 11.5% of imported patients in Taiwan had joint pain, while it was 100% and 98% in India and Reunion Island, respectively [20]. The extent of clinical symptoms may be increased with age. Severe complication may occur in patients over 40 years old and atypical infection symptoms, including encephalitis, seizure and neurologic diseases, may be seen in patients over 65 years old [21].

### Epidemiology

The epidemic situation of Chikungunya fever becomes more and more severe in recent

years. Over 20,000 confirmed cases were recorded in Lampung area, Indonesia, in the first 8 weeks of 2010. Cases were also found in Thailand and Madagascar in 2010 (Table 3). In Taiwan, Chikungunya fever was screened at international airports since March, 2006, and it was categorized as a notifiable disease since October, 2007. In this time frame, there were 2 imported Chikungunya fever cases found in Taiwan [22]. The first case was a 13 years old student. This patient studied abroad in Singapore in 2005 and visited relatives in Shanghai from July to August, 2006. He then returned to Singapore and came back to Taiwan on November 20 in the same year. During fever screening at airports, he had clinical signs of fever and cutaneous rash at lower limbs. Quarantine officers took samples

**Table 1. Symptom difference between Chikungunya fever and Dengue fever**

Features	Chikungunya fever	Dengue fever
Fever $\geq$ 40°C	Acute	moderate
Duration of fever	1- 2 days	5-7 days
Maculopapular rash	Often	Seldom
Shock, bleeding	Seldom	Less often
Arthritis	Often, last for few weeks	Seldom, shorter duration
Leucopenia	Often	Seldom
Thrombocytopenia	Seldom	Often

**Table 2. Comparison of clinical symptoms of Chikungunya fever in different epidemics (%)**

event signs	India 2006 (N = 876)	Reunion Island 2005-2006 (N = 504)	Malaysia 1998 (N = 51)	Taiwan 2007-2010.3 (N = 26)
	Fever	100	100	100
Joint pain or arthritis	98	100	78	11.5
Cutaneous rash	*	39	50	19.2
Headache	*	70	50	11.5
Myelalgia	*	*	50	*
Myalgia	*	60	50	7.7

\*None recorded

for laboratory examination and revealed PCR positive of Chikungunya fever. The second case was a 5 years old child. This patient visited relatives in Indonesia from May 22 to June 20, 2007. Quarantine officers at fever screening took sample for laboratory

examination for Dengue fever and malaria due to clinical symptoms of fever and generalized cutaneous rash. The results of Dengue fever and malaria were negative on June 22, but it was confirmed as Chikungunya fever by PCR on June 25.

**Table 3. Epidemic situation of Chikungunya fever in Southeast Asia and Europe**

Country	Year	Summary
Thailand[23]	1970	Confirmed cases found in Bangkok
	1988	Sporadic occurrence
	1995	Epidemic occurred in rainy season
	2008 (October)	40 confirmed cases found in a village in Narathiwat Province; CHIKV isolated from <i>Ae. albopictus</i> (Skuse) captured in this village.
	2009	5,233 confirmed cases
	2010 (January to February)	344 confirmed cases
Malaysia[24]	2008	4,271 confirmed cases
	2009	5,233 confirmed cases
	2010 (the first 6 weeks)	365 confirmed cases
Philippines[25]	1986	Chikungunya fever was found in team members of American Peace Corps
	1996	CHIKV antibody was detected in 216 people in Indang village; 156 villagers had IgM antibody
Indonesia[26]	1779	First epidemic recorded in Batavia area (Jakarta)
	1973	Epidemic occurred in Samarinda and Balikpapan
	1983	Epidemic in Island of Java with incidence of 70-90%
	1982 to 1985	8 epidemics occurred in the country
	2001 to 2003	Several epidemics
	2010 (January to February)	Over 20,000 confirmed cases in Lampung area
India[27-28]	2006	1,390,322 reported cases, in which 2,001 confirmed cases; the pathogen was Central/East African genotype CHIKV
	2007	59,535 reported cases with 1,826 confirmed cases
	2008	95,091 reported cases with 2,461 confirmed cases
	2009 (first half of the year)	21,977 reported cases with 2,258 confirmed cases
Singapore[29]	2008	690 confirmed cases
	2009	351 confirmed cases
Vietnam[30]	1966	10 confirmed cases found in 93rd Evacuation Hospital in southern Vietnam
Sri Lanka[31]	2008	1,300 confirmed cases in Moneragala area 1,106 confirmed cases in Embilipitiya area 200 confirmed cases in Polonnaruwa area
Madagascar[32]	2010 (February)	2,000 confirmed cases in Mananjary area
Japan[33]	2009 (January)	1 imported case (Malaysian female, Malaysia was the infection site)
Italy[34]	2007	334 suspected cases and 204 confirmed cases. The first confirmed case was a foreign traveler from India entering Italy on June 21. Clinical symptoms of Chikungunya fever were noted on June 23. Only one mortality case (83 years old male) was reported. The last confirmed case was reported in Rimini area on September 28. No new patient was reported since October. Fever was the most common clinical symptom, followed by weary and joint pain.

According to the data of Taiwan CDC Surveillance System, 88 cases were recorded from October 2007 to March 2010, including 1 case reported by medical facility and others reported by active surveillance system. There were 26 imported confirmed cases, including 2 cases in 2007, 9 cases in 2008, 9 cases in 2009 and 6 cases in 2010 (January to March) (Table 4). In these 26 cases, 23 were reported from fever screening station at international airports. Another 2 cases had contact history with Dengue patient and were confirmed as Chikungunya fever through blood examination by Taiwan CDC. Of these 2 cases, one was infected by Chikungunya fever and Dengue fever simultaneously. The other one was reported by one medical facility (samples were collected at the airport, but reported by medical facility before examination result presented). The countries of infection for all patients included Indonesia (14 cases), Malaysia (6 cases), Thailand (2 cases), India (1 case), Bangladesh (1 case) and Singapore (1 case).

The country of infection could not be determined in one case because this patient travelled in Indonesia and America successively.

From January 2006 to February 2009, 14 cases were detected by fever screening at international airports (13 at Taoyuan and 1 at Kaohsiung). Through gene sequence examination, Asian genotype was confirmed in all 7 patients came from Indonesia. East/Central/South African genotype was revealed in the other 7 cases (4 from Malaysia, 1 from Bangladesh, 1 from India and 1 from Singapore). Furthermore, E1-A226V gene mutation was found in the 4 cases from Malaysia and 1 case from Bangladesh. No West African genotype was noted [35-36] (Table 5).

### Risk Evaluation of Chikungunya Fever in Taiwan

#### A. International communication

In recent years Taiwan citizens frequently visiting Southeast Asian countries

**Table 4. Confirmed Chikungunya fever cases from October 2007 to March 2010**

Year	Case No.	Confirmed Patients			
		Taiwan nationality	Foreign spouse	Foreign laborer	Other foreigners
2007	2	-	-	1	1
2008	9	3	-	1	5
2009	9	3	1	2	3
March 2010	6	3	1	2	-

**Table 5. Genotyping result of CHIKV, from January 2006 to February 2009**

Country origin	Case No.	Genotype
Indonesia	7	Asian genotype
Bangladesh	1	East/Central/South African genotype
Malaysia	4	East/Central/South African genotype
India	1	East/Central/South African genotype
Singapore	1	East/Central/South African genotype

and the number of tourists in Taiwan is also increased. Thus, the risk of importing infectious disease is increased gradually. For example, the number of imported Dengue fever case was gradually elevated (Figure 2) and local Dengue fever epidemic was evidently correlated with imported pathogen, which indicated that risk of pathogen invading into Taiwan may be affected by international disease situation. According to Taiwan CDC database, more and more imported Chikungunya fever cases were recorded and the risk of CHIKV invasion into Taiwan cannot be neglected.

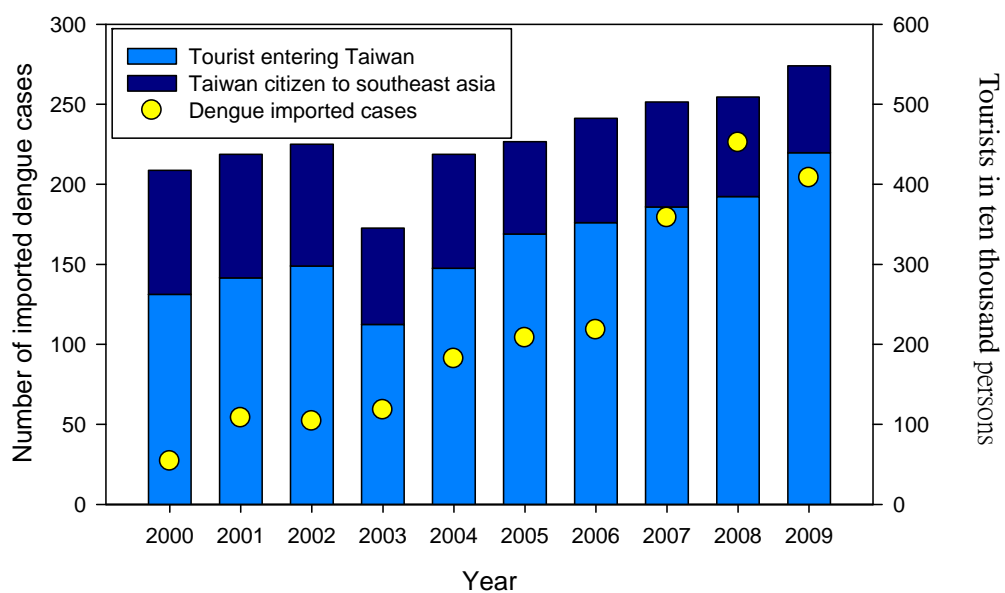
**B. Difficulty of differential diagnosis between Chikungunya fever and Dengue fever**

Clinical symptoms of these 2 diseases are very identical. However, incubation time of Chikungunya fever is shorter than the other disease. Asymptomatic patients are not rare, which is approximately 25% of all infected patients [37]. Since Chikungunya fever was categorized as a notifiable disease in October

2007, 73 cases were suspected and reported by medical facilities. Only 1 imported case was confirmed till 2009 and no indigenous case was detected. Thus, the alertness of medical staffs and authorities may be impaired due to these reasons.

**C. Citizen cognition and vector ecology**

Since Chikungunya fever was just categorized as a notifiable disease in October 2007 and the health education was mainly focus on Dengue fever prevention in the past and less on Chikungunya fever; thus, citizens may easily neglect this disease. Taiwan citizens are familiar with Dengue fever and also understand the prevention measures for this disease. Due to identical clinical symptoms as well as transmission vector of these 2 diseases and citizen cognition with Dengue fever, the risk of Chikungunya fever infection may be decreased. The transmission vectors in Asian areas are *Ae. aegypti* (L.) and *Ae. albopictus* (Skuse). In the epidemic event in Reunion Island in 2005-2006, the vector was *Ae. albopictus* instead of *Ae. Aegypti*.



**Figure 2. The number of departure Taiwan citizen to Southeast Asia, tourist entering Taiwan, and imported Dengue fever cases from 2000 to 2009**

CHIKV infection rate in saliva gland of *Ae. albopictus* (Skuse) was increased due to E1-A226V gene mutation in the virus. This characteristic elevated the transmission rate of this disease with *Ae. albopictus* (Skuse) and decreased mid gut infection rate in *Ae. Aegypti* (L.) Both of the vectors can be found in Taiwan, in which *Ae. albopictus* (Skuse) distributes within whole Taiwan area. Thus, there is high risk in Chikungunya fever epidemic if prevention procedures could not be conducted effectively while this disease invading Taiwan. *Ae. Aegypti* (L.) can only be found at Budai Township, Chiayi County and further southern Taiwan areas. If Chikungunya fever is transmitted by *Ae. Aegypti* (L.), the risk of transmission in southern Taiwan counties is higher than northern Taiwan areas. On the other hand, there is no risk difference in disease transmission if Chikungunya fever is transmitted by *Ae. albopictus* (Skuse). However, further evaluation is still needed if the risk of transmission is higher in southern Taiwan than in northern Taiwan if both mosquito species being the vectors (both species can be found in southern Taiwan).

### **Prevention strategy for Chikungunya fever in Taiwan**

#### **A. Enhance health education and public warning**

The public is unfamiliar to Chikungunya fever and its clinical signs although Chikungunya fever and Dengue fever are similar. Thus, in order to enhance public alertness to this disease, the current health education resources used on Dengue fever was applied for Chikungunya fever. Similar to

the case of Dengue fever, a cash reward of 2,500 NTD is offered for reporting of Chikungunya fever. The reward will be given to a citizen who voluntarily accepts Chikungunya fever screening test and is confirmed as imported or indigenous Chikungunya fever patient.

#### **B. Conduct medical education and training to improve diagnosis and treatment ability**

Clinical symptoms are similar in these 2 diseases; however, the extent is different (Table 1). Furthermore, various clinical signs may be found in different areas with different genotypes of virus (Table 2). It is necessary to conduct further education and provide international disease information for medical staffs to enhance differential diagnosis abilities for Chikungunya fever and Dengue fever, and to strengthen alertness of medical staffs for this disease. The risk of disease transmission can be reduced with promptly report of suspected patient in medical facilities and punctual prevention measures. Chikungunya fever related information had been fitted into the "Manual of clinical symptoms, diagnosis and treatment for dengue fever/dengue hemorrhagic fever". In addition, reward measures for medical staffs in reporting Chikungunya fever had also been added into "Regulations Governing Awards for the Control of Communicable Diseases".

#### **C. Continuously monitor transmission vector and control warning information**

The frequency of vector mosquitoes' investigation had been stipulated in the "Guidelines for dengue fever prevention". The vector information of Chikungunya fever can be handled simultaneously through



Dengue fever investigation. In order to reduce risk of infection, it is important to inform village heads proceeding vector mosquito elimination work when the vector density increased.

#### **D. Establish epidemiologic information and Grasp the trend of the epidemic**

It is not easy to monitor and diagnose this disease due to similar symptoms to Dengue fever. Oversight of this disease could occur if differential diagnosis is based on clinical signs only. Diagnosis accuracy can be improved with laboratory examination. Sample for Dengue fever examination will be tested for Chikungunya fever to enhance disease monitoring. Furthermore, serum epidemiologic investigation for Chikungunya fever is programming in order to understand the epidemiologic situation of this disease in Taiwan.

#### **E. Strengthen quarantine procedure preventing epidemic event**

At present, only imported Chikungunya fever cases were confirmed in Taiwan. No indigenous patient was found. Taiwan citizens should be reminded for self-protection measures while planning to visit Chikungunya fever epidemic areas or countries. Fever screening to people come back from these areas or countries should be continuously proceeded. Quarantine officers would provide mosquito net, mosquito spray and related health information to reduce the risk for virus transmission.

#### **Conclusion**

Presently samples from people with clinical signs are collected at fever screening station of international port for examination

according the epidemics of the country of infection. In order to reduce the risk of Chikungunya fever invasion into Taiwan through asymptomatic or subclinical infectious patients, citizens who come back from Chikungunya fever epidemic areas should be encouraged to receive blood examination actively. Diseases control authorities should implement transmission vector elimination and monitor work, enhance public health education, proceed medical staff training and establish response procedures to ensure public's health.

#### **References**

1. Lumsden W. An epidemic of virus disease in Southern Province, Tanganyika territory, in 1952–1953 II. General description and epidemiology. *Trans R Soc Trop Med Hyg* 1955; 49:15-57.
2. Outbreak and spread of chikungunya. *Wkly Epidemiol Rec* 2007;82:409-15.
3. Sudeep AB, Parashar D. Chikungunya: an overview. *J Biosci* 2008;33:443-9.
4. ProMED. Chikungunya - Italy (Emilia Romagna) (05). Available at: [http://www.promedmail.org/pls/otn/f?p=2400:1001:::NO::F2400\\_P1001\\_BACK\\_PAGE,F2400\\_P1001\\_PUB\\_MAIL\\_ID:1000%2C39363](http://www.promedmail.org/pls/otn/f?p=2400:1001:::NO::F2400_P1001_BACK_PAGE,F2400_P1001_PUB_MAIL_ID:1000%2C39363)
5. Robinson MC. An epidemic of virus disease in Southern Province, Tanganyika Territory, in 1952-53. I. Clinical features. *Trans R Soc Trop Med Hyg* 1955; 49:28-32.
6. Ross RW. The Newala epidemic. III. The virus: isolation, pathogenic properties and relationship to the epidemic. *J*

- Hygiene 1956;54:177-91.
7. Laras K, Sukri NC, Larasati RP, et al. Tracking the re-emergence of epidemic chikungunya virus in Indonesia. *Trans R Soc Trop Med Hyg* 2005;99:128-41.
  8. Dubrulle M, Mousson L, Moutailler S, et al. Chikungunya virus and *Aedes* mosquitoes: saliva is infectious as soon as two days after oral infection. *PLoS One* 2009;4:e5895.
  9. Tsetsarkin KA, Vanlandingham DL, McGee CE, et al. A single mutation in chikungunya virus affects vector specificity and epidemic potential. *PLoS Pathog* 2007;3:e201.
  10. Vazeille M, Moutailler S, Coudrier D, et al. Two Chikungunya isolates from the outbreak of La Reunion (Indian Ocean) exhibit different patterns of infection in the mosquito, *Aedes albopictus*. *PLoS ONE* 2007;2:e1168.
  11. Hammon WM, Rudnick A, Sather GE. Viruses associated with epidemic hemorrhagic fevers of the Philippines and Thailand. *Science* 1960;131:1102-3.
  12. Diallo M, Thonnon J, Traore-Lamizana M, et al. Vectors of Chikungunya virus in Senegal: current data and transmission cycles. *Am J Trop Med Hyg* 1999;60:281-6.
  13. Tesh RB, Gubler DJ, Rosen L. Variation among geographic strains of *Aedes albopictus* in susceptibility to infection with chikungunya virus. *Am J Trop Med Hyg* 1976;25:326-35.
  14. Turell MJ, Beaman JR, Tammariello RF. Susceptibility of selected strains of *Aedes aegypti* and *Aedes albopictus* (Diptera: Culicidae) to chikungunya virus. *J Med Entomol* 1992;29:49-53.
  15. Powers AM, Brault AC, Tesh RB, et al. Re-emergence of Chikungunya and O'nyong-nyong viruses: evidence for distinct geographical lineages and distant evolutionary relationships. *J Gen Virol* 2000;81:471-9.
  16. Reiter P, Fontenille D, Paupy C. *Aedes albopictus* as an epidemic vector of chikungunya virus: another emerging problem? *Lancet Infect Dis* 2006;6:463-4.
  17. Wu J-W, Teng H-J, Lin C, et al. Recent distribution of vector mosquitoes and epidemiology of the diseases they transmitted in Taiwan. *Med Entomol Zool* 2009;60:241-52.
  18. Brouard C, Bernillon P, Quatresous I, et al. Estimated risk of Chikungunya viremic blood donation during an epidemic on Reunion Island in the Indian Ocean, 2005 to 2007. *Transfusion* 2008;48:1333-41.
  19. Lenglet Y, Barau G, Robillard PY, et al. Chikungunya infection in pregnancy: Evidence for intrauterine infection in pregnant women and vertical transmission in the parturient. Survey of the Reunion Island outbreak. *J Gynecol Obstet Biol Reprod* 2006;35:578-83.
  20. Powers AM, Logue CH. Changing patterns of chikungunya virus: re-emergence of a zoonotic arbovirus. *J Gen Virol* 2007;88:2363-77.
  21. Economopoulou A, Dominguez M, Helynck B, et al. Atypical Chikungunya virus infections: clinical manifestations, mortality and risk factors for severe disease during the 2005-2006 outbreak

- on Reunion. *Epidemiol inf* 2009; 137: 534-41.
22. Wu JW, Lee TC, Hunag TM, et al. The First Imported Case of Chikungunya Fever in Taiwan. *Taiwan Epidemiol Bull* 2007;23:236-41.
23. Thailand MoPH. Disease surveillance and investigation 2010. Available at: [http://epid.moph.go.th/chikun/chikun/situation/y52/chikun\\_200912301520.pdf](http://epid.moph.go.th/chikun/chikun/situation/y52/chikun_200912301520.pdf)
24. Malaysia M. Situasi Semasa Demam Denggi Dan Chikungunya Di Malaysia. Available at: <http://jknterengganu.moh.gov.my/v3/modules/news/article.php?storyid=102>
25. Retuya TJA, Ting DL, Dacula BD, et al. Chikungunya fever outbreak in an agricultural village in Indang, Cavite, Philippines. *Phil J Microbiol Infect Dis* 1998;27:93-6.
26. Siregar DSD. Chikungunya Hits Hard in Rainy Season. *The Jakarta Globe* 2010. Available at: <http://www.thejakartaglobe.com/news/chikungunya-hits-hard-in-rainy-season/362940>
27. Mavalankar D, Shastri P, Raman P. Chikungunya epidemic in India: a major public-health disaster. *Lancet Infect Dis* 2007;7:306-7.
28. State-wise Status of Chikungunya Fever in India. Available at: <http://www.nvbdc.gov.in/Doc/chikun-update07.pdf>
29. Ministry of Health S. MOH weekly publication of statistics on local infectious disease situation. Available at: [http://www.moh.gov.sg/mohcorp/uploadedFiles/Statistics/Infectious\\_Diseases\\_Bulletin/2009/2009\\_week\\_52.pdf](http://www.moh.gov.sg/mohcorp/uploadedFiles/Statistics/Infectious_Diseases_Bulletin/2009/2009_week_52.pdf)
30. Deller JJ, Russell PK. An analysis of fevers of unknown origin in American soldiers in Vietnam. *Ann Intern Med* 1967;66:1129-43.
31. ProMED. Chikungunya (02): Sri Lanka, Indonesia. Available at: [http://www.promedmail.org/pls/otn/f?p=2400:1202:4897455746564981::NO::F2400\\_P1202\\_CHECK\\_DISPLAY,F2400\\_P1202\\_PUB\\_MAIL\\_ID:X,75561](http://www.promedmail.org/pls/otn/f?p=2400:1202:4897455746564981::NO::F2400_P1202_CHECK_DISPLAY,F2400_P1202_PUB_MAIL_ID:X,75561)
32. ProMED. Chikungunya (10): Madagascar. Available at: [http://www.promedmail.org/pls/otn/f?p=2400:1202:53103::NO::F2400\\_P1202\\_CHECK\\_DISPLAY,F2400\\_P1202\\_PUB\\_MAIL\\_ID:X,81871](http://www.promedmail.org/pls/otn/f?p=2400:1202:53103::NO::F2400_P1202_CHECK_DISPLAY,F2400_P1202_PUB_MAIL_ID:X,81871)
33. ProMED. Chikungunya: Japan ex Malaysia. Available at: [http://www.promedmail.org/pls/otn/f?p=2400:1202:4897455746564981::NO::F2400\\_P1202\\_CHECK\\_DISPLAY,F2400\\_P1202\\_PUB\\_MAIL\\_ID:X,75969](http://www.promedmail.org/pls/otn/f?p=2400:1202:4897455746564981::NO::F2400_P1202_CHECK_DISPLAY,F2400_P1202_PUB_MAIL_ID:X,75969)
34. Rezza G, Nicoletti L, Angelini R, et al. Infection with chikungunya virus in Italy: an outbreak in a temperate region. *Lancet* 2007;370:1840-6.
35. Huang JH, Yang CF, Su C-L, et al. Imported chikungunya virus strains, Taiwan, 2006-2009. *Emerg Infect Dis* 2009;15:1854-6.
36. Shu PY, Yang CF, Su CL, et al. Two imported chikungunya cases, Taiwan. *Emerg Infect Dis* 2008;14:1326-7.
37. Sissoko D, Moendandze A, Malvy D, et al. Seroprevalence and risk factors of chikungunya virus infection in Mayotte, Indian Ocean, 2005-2006: a population-based survey. *PLoS ONE* 2008;3:e3066.

## **An Overview in the Primary Stage of Novel Influenza A (H1N1) Epidemic in Eastern Taiwan and Its Revelation**

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### **Abstract**

In the primary stage of the epidemic of novel influenza A (H1N1) in Eastern Taiwan, 2009, a total of 11 novel influenza A (H1N1) cases were reported in accordance with the investigation case definition. One was positive and the other 10 were excluded. Of the 10 excluded cases, one was confirmed as dengue fever. In June 2009, 149 specimens were collected through the H1N1 community surveillance in Eastern Taiwan by sentinel physicians, one seasonal influenza A (H3) and one novel influenza A (H1N1) were confirmed. In July (as of July 16), 72 specimens were tested, 2 seasonal influenza A (H3) and 5 novel influenza A (H1N1) were confirmed. A total of 221 specimens were collected from June 1 to July 16, 3 seasonal influenza A (H3) and 6 novel influenza A (H1N1) were confirmed but all of patients' symptoms were mild, of which 5 were imported cases and 1 indigenous case without travel history. From week 27 to week 29, the proportion of novel influenza A (H1N1) virus in all positive cases in community surveillance in eastern Taiwan was 71.4%, which was lower than the surveillance

proportion 88.2% in Taiwan area.

What were learnt from the primary stage of the epidemic and the prevention of novel influenza A (H1N1) in Eastern Taiwan are as following: (1) The community-based prevalence rate of novel influenza A (H1N1) virus is slightly lower than the rate in Taiwan area, but there is a clearly upward trend; (2) One who develops with non-specific flu symptoms and has a travel history, the possibility of dengue and chikungunya fever must be considered, and the specimens should be taken for further testing as far as possible; and (3) To follow-up the confirmed case that has no travel history; to those seriously-ill, death and cluster cases, intensified monitoring is needed in order to alleviate the impact on public health.

**Keywords:** novel influenza A (H1N1), imported, dengue fever

### **Introduction**

At end of March to early April 2009, an outbreak of novel influenza A (H1N1) occurred in Mexico [1]. This pandemic was caused by a novel influenza A (H1N1) virus which was the product of 4 virus strains after genetic recombination. These 4 virus strains contained 2 swine flu virus strains, 1 human flu virus strain and 1 avian flu virus strain [2-3]. The incubation period is around 1 to 4 days. Once people are infected, the virus could be transmitted from one day before the onset of symptoms to the day before fever relieved [4]. The patient's symptom is similar to seasonal flu, which including fever, cough, sore throat, fatigue and headache. Vomiting and diarrhea are usual but not common to the

patients of seasonal flu [5]. The droplets would be produced when patients are sneezing or coughing, and the flu viruses would be spread by close contact between people or come into contact with contaminated fomites [6]. Later, the epidemic was brought out through aircraft transmission and rapidly spread to many countries such as the United States and Canada [7].

The novel influenza A (H1N1) outbreak was occurred in Mexico in April 2009. One novel influenza A (H1N1) confirmed Mexican took MU 505 flight of Eastern Airline from Mexico to Hong Kong via Shanghai on April 30; 24 passengers on the same flight transferred to Taiwan on May 1. Six of them had traveled to Hualien and Taitung areas on May 2. The scheduled itinerary was cancelled after urgent connections and they were directly sent to the Hualien Hospital, Department of Health. Those close contacts of novel influenza A (H1N1) confirmed cases were arranged in the quarantine wards and preventive medication were given. Till the afternoon of May 3, the isolation was relieved after the laboratory results were negative. On May 18, a foreign physician who served in Taitung had a fever when he entered Taiwan from Hong Kong. He has been working on a cruise as a doctor in New York, USA, from February 2009 to May. He was reported as a H1N1 novel influenza investigation case when he entered Taiwan and was sent to the negative pressure isolation ward in Taoyuan Hospital for further treatment. The test result showed that he was the first novel influenza A (H1N1) confirmed case in Taiwan.

The amended classification of infectious

diseases was proclaimed in Taiwan on April 27, 2009. Novel influenza A (H1N1) virus infection was added into category 1 communicable diseases. World Health Organization (WHO) upgraded the influenza A (H1N1) virus infection to level six of global pandemic on June 11, 2009. It meant the virus has caused a wide-spreading community infection to at least two continents around the world [8]. However, this global pandemic is moderate. As a result, Taiwan has proclaimed to delete novel influenza A (H1N1) virus infection from category 1 communicable diseases on June 19, 2009. People who suffered from influenza with severe complications and affected with novel influenza H1N1 virus would be managed in accordance with the time period to report, reporting and related preventive regulations of category 4 communicable diseases.

Taiwan was gradually affected by this epidemic since May of 2009. This study describes the epidemic and prevention of novel influenza A (H1N1) virus infection in Eastern Taiwan (including Hualien and Taitung County) in the primary stage of the epidemic.

## Materials and Methods

### A. Study Period

The study period is from April 30 to July 22, 2009, or week 18 to week 30. The calculation of Week is in accordance with WHO's method, that is, the first week is from January 1.

### B. Case definition

#### 1. Investigation case

Investigation case is defined as a case has

matching clinical conditions (with acute respiratory disease and fever, the clinical symptoms ranging from minor influenza-like illness to more serious pneumonia) and epidemiological conditions (the patient who has had a close contact with a confirmed case or a probable case, or has a travel history to the area where the residence region of confirmed case or probable case).

## 2. Probable case

Probable case is a case conforming to the clinical conditions and the test result is influenza A virus positive, but unable to subtype with the test methods of seasonal influenza; or a case with conformed clinical and epidemiological conditions, or death with unexplained acute respiratory symptoms, who has the epidemiological connection with the probable or confirmed cases.

## 3. Confirmed case

Confirmed case is a case has matching clinical conditions and the test results (real-time RT-PCR positive).

This study has incorporated and analyzed the cases who fitted with the definition of investigation case for novel influenza A (H1N1) and the confirmed cases from sentinel physician surveillance in Haulien and Taitung area during April 30 to July 22, 2009.

## C. Testing laboratories

At the beginning of novel influenza A (H1N1) epidemic, the investigation case and the close contact of confirmed case were tested with real-time RT-PCR at Taiwan CDC laboratory for confirmation. In order to accelerate the testing and in favor of the community-based surveillance, the technique

was transferred to the 10 contract laboratories in Taiwan from June 1, 2009.

## D. Preventive and control measures

The amended infectious diseases classification was announced by the Department of Health on April 27, 2009. Novel influenza A (H1N1) was added as category 1 communicable disease. The antiviral agents for novel influenza A (H1N1) reported case was included at government fund. Preventive prescription also included all close contacts of probable case or confirmed case. Every Branch office and emergency management hospital increased the stockpile of antiviral agents after the epidemic became more severe. On May 2, 2009, the guidelines announced that the hospital should take responsibility to isolate and treat the investigation case of novel influenza A (H1N1). This policy was amended on May 27, if there is a difficulty to schedule a ward, a home quarantine could be adopted for the minor cases after clinician's judgment. WHO announced the influenza A (H1N1) was upgraded to level six of global pandemic on June 11, 2009. This overall pandemic is moderate. Therefore, Taiwan has proclaimed to delete novel influenza A (H1N1) from category 1 communicable diseases on June 19, 2009. People who suffered from influenza with severe complications and infected with novel influenza H1N1 virus would be managed in accordance with the report deadline, and related preventive regulations of category 4 communicable diseases. In the meantime, to the mild confirmed cases of influenza A (H1N1) and their close contacts, the use of antiviral agents at government fund was cancelled.

## Results

### A. The epidemic scale and symptoms in Eastern area

A total of 11 cases were reported in accordance with the definition of investigation case of novel influenza A (H1N1). The distribution of symptoms was: fever (90.9%), cough (81.8%), running nose (18.2%), myalgia

(9.1%), headache (9.1%), vomiting (9.1%), diarrhea (9.1%), dyspnoea (9.1%) and pneumonia (9.1%).

### B. Laboratory findings

Among 11 novel influenza A (H1N1) investigation cases, one was confirmed as a novel influenza A (H1N1) positive; the other 10 cases were excluded (Table 1). Of those 10

**Table 1. The number of cases matched to the novel influenza A (H1N1) investigation case definition in Eastern Area, 2009**

		Hualien	Taitung	Total
H1N1 positive case		0	1	1
H1N1 negative case		9	1	10
Subtotal		9	2	11

No.	Date of report	Place of residence	Age	Sex	Screen method	Report hospital	Travel history	Test results of novel influenza A (H1N1)	Symptoms	Remarks
1	May 12	Hualien	21	Female	Airport Screening	Taoyuan Hospital	Canada	Negative	Fever, cough	Stay in Canada for years
2	May 18	Taitung	52	Male	Airport Screening	Taoyuan Hospital	USA	Positive	Fever, headache, cough	The first case in Taiwan
3	May 29	Hualien	67	Female	Reported by hospital	National Yang-Ming University Hospital	China	Negative	Fever, cough	
4	May 31	Hualien	29	Female	Reported by hospital	Mennonite Hospital in Hualien	Vietnam	Negative	Fever, cough, running nose	AH3 Flu family cluster
5	May 31	Hualien	53	Male	Reported by hospital	Mennonite Hospital in Hualien	China	Negative	Fever, cough	
6	June 1	Taitung	20	Female	Reported by hospital	National Cheng Kung University Hospital	USA	Negative	Fever, cough	
7	June 3	Hualien	26	Male	Reported by hospital	Hualien Hospital, DOH	Thailand	Negative	Fever, vomiting, diarrhea	Dengue confirmed case
8	June 3	Hualien	34	Male	Reported by hospital	Hualien Hospital, DOH	China	Negative	Fever, myalgia	
9	June 10	Hualien	23	Female	Reported by hospital	Hualien Hospital, DOH	Thailand	Negative	Fever, cough, running nose	
10	June 12	Hualien	63	Male	Reported by hospital	Linkou Chang Gung Memorial Hospital	Philippines	Negative	Cough, dyspnea, pneumonia	Stay in Philippines for years
11	June 16	Hong Kong	27	Female	Reported by hospital	Hualien Tzu Chi Hospital	Hong Kong	Negative	Fever, cough	

negative cases, one was a male university student who returned from Thailand. The symptoms developed at the same day on his return. He went to see a doctor and Tamiflu was taken, but he was still suffering from high fever after 5 days. Then he was reported as a suspected dengue fever case by another doctor during follow-up treatment. The specimen was taken and tested positive for dengue NS1 antigen and PCR by CDC laboratory.

A total of 149 specimens were collected through the sentinel H1N1 community-based surveillance. One seasonal influenza A H3 and 1 novel influenza A (H1N1) were confirmed; 72 specimens were collected in July (as of July 16), 2 seasonal influenza A H3 and 5 novel influenza A (H1N1) were confirmed; a total of 221 specimens were collected from the early June to July 16, 3 seasonal influenza A H3 and 6 novel influenza A (H1N1) were confirmed.

#### C. Effectiveness of novel influenza A (H1N1) prevention and control

Due to the effectiveness of “Blocking strategy” at the early stage of the epidemic, the first imported confirmed case was isolated

before entering Taiwan. Accordingly, no indigenous case and community infection was found in Eastern Taiwan during novel influenza A (H1N1) was listed as category 1 communicable diseases. From June 19 to July 16, 2009, 6 novel influenza A (H1N1) confirmed cases were detected by sentinel surveillance system in Eastern area (Table 2). All of 6 cases were moderate. Five were imported cases, 1 was from the United States, 1 was from Thailand and 3 were from Korea (a family cluster, it was suspected that they were infected while travelling in Korea), the other one was an indigenous case without travel history. A total of 130 pills (Tamiflu) were used, 40 pills for therapeutic use (4 investigation cases), and 90 pills were used for the close contacts (9 persons) of confirmed cases as preventive medication.

#### Discussion and Conclusion

A. There was a gradual increasing trend on novel influenza A (H1N1) epidemic in Eastern area: As of July 22, 2009, there were 94 novel influenza A (H1N1)

**Table 2. The novel influenza A (H1N1) confirmed cases monitored by sentinel physicians in Hualien and Taitung area, 2009**

No.	Sex	Place of residence	Age	Travel history	Onset date	Sampling Hospital	Sampling date	Confirmed date	Remarks
1	Male	Pingtung	15	USA	June 21	Hualien Tzu Chi Hospital	June 23	July 3	Imported
2	Female	Taitung	17	Thailand	July 3	Taitung Christian Hospital	July 4	July 7	Imported
3	Male	Hualien	14	Korea	July 9	Hualien Hospital, DOH	July 12	July 14	Imported, family cluster
4	Female	Hualien	43	Korea	July 9	Hualien Hospital, DOH	July 15	July 17	Imported, family cluster (mother of case 3)
5	Female	Hualien	12	Korea	July 9	Hualien Hospital, DOH	July 15	July 17	Imported, family cluster (sister of case 3)
6	Female	Hualien	6	None	July 19	Joy Clinic	July 20	July 22	Indigenous case without travel history



confirmed cases in Taiwan, only one was a severe case, the rest were mild. From week 27 to week 29 (June 28 to July 18), the proportion of novel influenza A (H1N1) virus in Taiwan community was 88.2%; in the meantime, a total of 6 novel influenza A (H1N1) cases were confirmed in Eastern area but all of their symptoms were mild. During this period, the proportion of novel influenza A (H1N1) virus in Eastern Taiwan community was 71.4%, which was slightly lower than the proportion in Taiwan area. However, it was obviously higher than the proportion (50%) in week 24 to week 26 (June 7 to 27). It indicated that the trend was gradual increasing on the proportion of novel influenza A (H1N1) virus.

B. One who develops non-specific flu symptoms and with a travel history, the possibility of dengue and chikungunya fever must be considered, and the specimens are needed to be taken for further test if possible. A total of 103 dengue fever cases were confirmed in Taiwan till July 22, 2009, only one was indigenous case and the other 102 were imported cases. Among them, 50 cases were from Indonesia, 25 cases were from Vietnam, 6 cases were from Thailand, and 21 cases were from other countries. It showed that among Taiwan's neighboring countries, especially the countries in Southeast Asia, was not only the epidemic area of novel influenza A (H1N1), but also was the dengue fever prevalent area. One university student was reported as an investigation case of novel influenza A (H1N1), but later he

was confirmed as a dengue fever case. He traveled to Thailand during May 23 to 28. After returning to Taiwan, he had vomiting and diarrhea on May 30. He went to Mennonite Christian Hospital for medical treatment the next day. The doctor prescribed Tamiflu but the symptoms were not alleviated and a fever was developed. He went to a clinic and was reported as a novel influenza A (H1N1) investigation case on June 2 and was isolated at the Hualien Hospital, the Department of Health. He was reported as a dengue fever case and the specimen was taken for test, both the results of dengue NS1 antigen and RT-PCR were positive.

C. To follow-up the confirmed case who has no travel history, especially the seriously-ill, death and cluster cases need intensified monitoring: A 6 year-old girl had a fever and was sent to a clinic for treatment on July 19, the specimen was taken for test by a sentinel physician and the novel influenza A (H1N1) was confirmed on July 22. The case's mother is a Vietnamese, who went to Vietnam on July 12, 2009 but did not return. The rest of the girl's relatives had no history of travel abroad. It showed that the novel influenza A (H1N1) virus had quietly slipped into the community. The proportion of novel influenza A (H1N1) virus was gradually over passing the seasonal flu, it will become the mainstream in the future flu season. Therefore, for the seriously-ill, death and cluster cases, intensified monitoring is needed in order to alleviate the impact on public health.

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### References

1. CDC. Update: novel influenza A (H1N1) virus infections - worldwide, May 6, 2009. *MMWR* 2009;58:453.
2. Dawood FS, Jain S, Finelli L, et al. Emergence of a novel swine-origin influenza A (H1N1) virus in humans. *N Engl J Med* 2009; 360:2605.
3. Trifonov V, Khiabani H, Rabadan R. Geographic dependence, surveillance, and origins of the 2009 influenza A (H1N1) virus. *N Engl J Med* 2009;361:115-9.
4. CDC. Interim guidance on specimen collection, processing, and testing for patients with suspected swine-origin influenza A (H1N1) virus infection. <http://www.cdc.gov/h1n1flu/specimencollection.htm>
5. WHO. Human infection with new influenza A (H1N1) virus: clinical observations from Mexico and other affected countries, May 2009. *Weekly epidemiological record* 2009;84:185-96.
6. CDC. Interim guidance on antiviral recommendations for patients with novel influenza A (H1N1) virus infection and their close contacts. <http://www.cdc.gov/h1n1flu/recommendations.htm>
7. Khan K, Arino J, Hu W, et al. Spread of a novel influenza A (H1N1) virus via global airline transportation. *N Engl J Med* 2009;361 :212-4.
8. WHO. World now at the start of 2009 influenza pandemic. [http://www.who.int/mediacentre/news/statements/2009/h1n1\\_pandemic\\_phase6\\_20090611/en/index.html](http://www.who.int/mediacentre/news/statements/2009/h1n1_pandemic_phase6_20090611/en/index.html)