Taiwan Epidemiology Bulletin

August 9 , 2011/ Vol.27 / No.15

Outbreak Investigation Express

Shigellosis Outbreak in the Disabled Education Institute, March – May, 2011

Hsuan-Chih Lin[1], Hsiao-Ping Tung[1], Wan-Chin Chen[1], Huai-Te Tsai[2,3], Dah-Shyong Jiang[2], Tsuey-Fong Lee[4], Hwan-Feng Wang[1], Chun-Ling Lai[1]

1. First Branch, Centers for Diseases Control, Taiwan
2. Field Epidemiology Training Program, Centers for Diseases Control, Taiwan
3. Sixth Branch, Centers for Diseases Control, Taiwan
4. Maternal, Infant and Reproductive Health Division, Bureau of Health Promotion, Taiwan

Abstract

During March 7 - May 16, 2011, three waves of shigellosis outbreaks occurred in the dormitories of the Disabled Education Institute in Yilan County. A total of 21 residents, 2 staff members, and 1 service draftee had symptoms of diarrhea. Shigellosis infection was confirmed in 12 residents and 1 staff member.

The epidemic curve, plotted by symptom onset dates of case-patients, indicates that the outbreak was likely propagated through person-to-person transmission. Control and preventive measures were applied. These included limiting contact between dormitories, assigning specific persons to clean and disinfect the dormitories, designating quarantine areas or infected case-patients, and closely monitoring daily health reports. As a result, disease transmission ceased on May 20th.

Key words: Shigellosis, Disabled Education Institute, outbreak

The Taiwan Epidemiology Bulletin series of publications is published by Centers for Disease Control, Department of Health, Taiwan (R.O.C.) since Dec 15, 1984.

Publisher : Feng-Yee Chang

Editor-in-Chief : Yi-Chun Wu

Executive Editor : Li-Gin Wu, Hsiu-Lan Liu

Telephone No : (02) 2395-9825

Address : No.6, Linshen S. Road, Taipei, Taiwan 100 (R.O.C.)

Website : http://teb.cdc.gov.tw/

Suggested Citation :

[Author].[Article title].Taiwan Epidemiol Bull 2011;27:[inclusive page numbers].

INSIDE

Original Article

Investigation of Japanese Encephalitis Confirmed Cases in South Taiwan, 2010

Ya-Lin Liu[1], Chin-Shyan Wang[1], Tsung-Wen Kuo[2], Sheng-Tang Wei[3], Yi-Chun Wu[4]

1. Fourth Branch, Centers for Disease Control, Taiwan
2. Abbott Laboratories Services Corp., Taiwan Branch
3. Fifth Branch, Centers for Disease Control, Taiwan
4. Chief Secretary Office, Centers for Disease Control, Taiwan

Abstract

In 2010, there were 8 Japanese encephalitis confirmed cases in south Taiwan (Yunlin County, Chiayi County/City, and Tainan County/City), with the first case occurring in late May and the remaining 7 cases occurring in June. Compared to the last 3 years, the prevalence of Japanese encephalitis in south Taiwan in 2010 was higher than the prevalence threshold of the same periods of the other years. With the purpose of serving as a reference for future investigations, this report documents the processes used and experiences gained from conducting an epidemic investigation of Japanese encephalitis in 2010. Confirmed cases and possible infection sources were investigatd; additionally, possible environmental risk factors for Japanese encephalitis cases were tallied, and the results showed that gutters and pigeon sheds were the most commonplace factors. Additionally, this report provided recommendations on prevention measures, such as thorough methodology of epidemic and environmental investigation, vaccination, health education and promotion, health monitoring, disease surveillance, visits to medical care institutions, and hanging mosquito lamp.

Keywords: Japanese encephalitis, environment investigation, mosquito lamp

Introduction

Japanese Encephalitis Virus (JEV) is from the genus *flavivirus* of the family *Flaviviridae*, and house mosquitoes are the disease vector. Many kinds of animals, such as human beings, pigs, monkeys, horses, cows, sheep, dogs and birds, can be infected. The transmission route of JEV is mainly through the following course: from wild or domestic birds to mosquitoes to pigs. Birds and pigs are the most important hosts that allow JEV to maintain, replicate and transmit. Pigs, also called amplifier hosts because of their high infection rates, high productivity, long post-infection viremia time, and high viral quantities in the blood, are an important source of JEV. Under normal circumstances, JEV only leads to symptoms in humans, pigs and horses. Once stung by a JEV-infected mosquito and infected with Japanese encephalitis, an infected person can expect an incubation period of about one to two weeks, with the vast majority of infection being indolent. The common clinical symptoms are fever, headache, and convulsion; more severe cases may lead to coma or death (mortality rate of about 25%). Half of the survivors may have neurologic sequelae, which are more common in children [1-2]. *Culex tritaeniorhynchus* and *Culex annulus*, the main vectors of JEV in Taiwan, live in paddy rice fields, water caves, irrigation ditches, and ponds. Since 1986, when comprehensive prophylactic vaccination of JEV for children was implemented in Taiwan, the number of children infected has decreased year by year while adults have become the main infection objects. There are two possible causes: (1) Comprehensive prophylactic vaccination of JEV for children; (2) Because of urbanization of rural areas and centralization of pig farmers, the chances of human exposure to vector mosquitoes have decreased year by year, while the number of highly susceptible elderly individuals has increased [3-5]. Current strategies for prevention and control of Japanese encephalitis include: prophylactic vaccination of JEV, control of animal hosts (e.g. inoculation of JEV for pigs and horses and moving animal farms away from residential districts), and vector mosquitoes control (e.g. release of larvicide in paddy fields) [1-3].

The prevalent season of Japanese encephalitis in Taiwan is from May through October annually, and the peak is usually in June and July. According to surveillance data of the CDC (calculated by date of disease onset), the number of national Japanese encephalitis confirmed cases of from 2007 to 2010 were 37, 17, 18, and 33, respectively, and the number of mortality cases were 2, 1, 1, and 2, respectively. The number of confirmed cases in south Taiwan between 2007 and 2010 were 7, 5, 0, and 8, respectively, with most occurring in May through July; in both 2008 and 2010, there was 1 death case.

In the afternoon of May 26, 2010, the first Japanese encephalitis confirmed case in south Taiwan for the year was reported via the notifiable disease reporting system, and the Fourth Branch of CDC contacted the Health Bureau of Tainan City immediately and asked it to launch an epidemic investigation of the case as soon as possible and to have the result reported back within 24 hours. The keys of this epidemic investigation included: the case's disease progression course, health status, inoculation history of Japanese encephalitis, medical history, as well as environmental investigation of the case's activity area during the period of communicability (including house) and the health statuses of the case's family and neighbors. Consequently, we were able to understand the progression of the case and identify the possible infection source. Furthermore, we were able to ascertain if the case became infected despite prior vaccine inoculation, and to rule out the possibility of cluster infection.

Based on the results of the epidemic and environment investigation, we can make an assumption about the possible infection source of the case. Then, by hanging mosquito lamps around nearby animal farms to catch vectors, we can strengthen the prevention measures and ascertain if the *Culex tritaeniorhynchus* caught were carriers of JEZ or not through laboratory examination. Furthermore, we gave health education to the individuals living around the suspected infection source, increased inoculation rates of Japanese encephalitis among children in those townships and villages, and strengthened the reporting systems and procedures in hospitals.

Materials and Methods

A. Investigation subjects and periods: Investigation subjects were selected through the notifiable diseases reporting system in Taiwan, focusing on the confirmed cases of non-imported Japanese encephalitis in south Taiwan. Data collection was based on the date of disease onset of the cases, ranging from Jan. 1, 2010, to Dec. 31, 2010.

B. Catching vectors by hanging the mosquito lamps:

   a. Methods: Mosquito lamps were hung near the suspected infection sources by healthcare personnel, and most were hung in bird or animal farms and under the eaves of buildings near the breeding grounds (e.g. paddy rice fields). The lamps were switched on from 5pm to dawn of the next day, and mosquitoes were collected and sent to the CDC investigation and testing center to indentify the species, and if *Culex tritaeniorhynchus* was caught, virus culture was performed to ascertain if JEV was present.

   b. Regarding the first Japanese encephalitis death case in southern Taiwan in 2010 (Case 1), we chose different pigsties around the case's workplace (Shiaying Township) to hang the mosquito lamps, and the lamps were marked by English alphabets A and B to represent the different pigsties. Pigsty A was closer to the activity area of the case than pigsty B, and A1 and A2 represented the same pigsty but different locations. Only 3 lamps were hung due to the limited number of mosquito lamps available.

   c. Because of the limited quantity of mosquito lamps, varying numbers of lamps, ranging from 1 to 3 were, hung for cases 2 to 8. To hang the lamps was evaluated by the local health authorities because hanging mosquito lamps is a suggestive prevention measure in the communicable diseases working manual.

C. Percentage of environmental risk factors: We took the number of confirmed cases with any environmental risk factor in their living or activity area during the period of communicability as numerator and used the 8 confirmed cases as denominator, and the value derived from this division was later multiplied by 100%.

Definition of Terms

A. Southern district: 5 Counties and Cities in total, including Yunlin County, Chiayi City, Chiayi County, Tainan City and Tainan County.

B. Reported Japanese encephalitis cases: Cased with any of the following conditions:

a. Conformed to clinical conditions: if the following acute neurologic symptoms occurred: fever, conscious disturbance, vomiting, neck stiffness, convulsion, dystonia, headache, meningeal signs, and mental symptoms (delirium, unconsciousness, etc.).
b. An epidemiologic relation with a confirmed case that was highly suspected by the doctor.

C. Japanese Encephalitis confirmed cases: Cases with positive results to any of the following tests:
a. Clinical specimens (tissue, cerebrospinal fluid or other body fluid) were isolated and JEV was identified.
b. The molecular nucleic acid test of clinical specimens showed positive results. Positive results of JEV-specific IgM antibody in cerebrospinal fluid.
c. JEV-specific IgM and/or IgG antibody positive in blood serum during acute phase (or first collection).
d. Under the condition of no recent inoculation record and excluding cross interaction of other *Flaviviridae*, the JEV-specific IgM and/or IgG antibody in paired sera (both recovering and acute phases) turned into positive or the amount increased to more than 4 times.

D. Suspected infection source: Japanese encephalitis vector mosquitoes breed mainly in paddy rice fields, drains, water reservoirs, ponds, and wetlands. The main hosts of JEV are animals and birds, with pigs as the major hosts for virus amplification. Because the vectors belong to *Culex*, they have kilometers of flying range. As a result, the environment investigation focused on searching the breeding grounds of the vector mosquitoes (eg. water reservoirs like paddy fields, ditches, and ponds, and check if any wrigglers of *Culex* exist) and the places house animals and birds (eg. pigsties and dove cottages) within a one kilometer circumference of the activity area of a confirmed case. Thus, if *Culex tritaeniorhynchus* was caught in the breeding grounds or places that house animals and birds within a one kilometer circumference of the activity area of a confirmed case, those places would be the suspected infection origin. If not, those places were excluded as infection sources.

E. Japanese encephalitis vaccination: If the confirmed case or the family couldn't be sure if the case has had the Japanese encephalitis vaccine and no record could be found through NIIS of the CDC, for cases 43 years of age or older (because regular Japanese encephalitis vaccination was implemented in Taiwan in 1968), they would be defined as having not been inoculated against Japanese encephalitis. For those under 43 years old, even if the confirmed case or the family could not be sure if the case has been inoculated against Japanese encephalitis and no record could be found through NIIS of the CDC, the case would be defined as having no record.

F. Risk factors for Japanese encephalitis infection: If a case conformed to any of the following definitions: having environmental risk factors (e.g. if Japanese encephalitis vector mosquitoes, paddy fields, ditches, birds or animals existed in the vicinity of the living or activity area of the confirmed case during the period of communicability); the confirmed case had not been inoculated against Japanese encephalitis vaccine or had no record of inoculation.

G. Epidemic threshold: Mean case numbers were calculated for each month from data of the same month, the month before and the month after in the last 3 years in the same district, with the addition of 2 standard deviations. For example, the epidemic threshold of Japanese encephalitis of southern district in June 2010 was 4.0 cases.【The result of 2007~2009 was analyzed from Table 3: Mean value was 1.22 cases, and the standard deviation was 1.39 cases】

Results

First Japanese encephalitis death case in South Taiwan in 2010

A. Background of the case: A 50-year-old female, living in Tainan City, was an accountant by occupation, with history of hypertension, had never been inoculated against Japanese encephalitis, lived with 3 people (including her husband, son, and daughter); her husband was 62 years old, and had never been inoculated, whereas the 2 children had.

B. Illness progression and medical course: On May 18, the case felt discomfort and told her friend that she would be fine after taking some rest; she did not go to a hospital immediately. On May 19, she went to a nearby clinic due to constant fever, dizziness, headache, and trance. On May 20, she was admitted into a nearby regional hospital. On May 21, she was emergently transmitted to a medical center due to signs of constant fever, convulsion, and unconsciousness. On May 24, the hospital reported her as a Japanese encephalitis case, which was confirmed by the investigation and testing center of CDC on May 26. The case died on June 3 due to unfavorable condition (cause of death was Japanese encephalitis with complication of respiration failure).

C. Investigation of activity area (including her house) during the period of communicability (investigated by the Public Bureau of Tainan City and Tainan County, along with the Fourth Branch of CDC): In the beginning, the husband said he did not know where the case worked at, and after several attempts of communication, he only revealed that the case worked near the industrial district in Shiaying Township, Tainan City, and insisted that he could not tell the name or the address due to personal reasons. Although he was informed that, according to the 43rd clause in law of prevention and treatment of infectious diseases, he could be fined if he refused to cooperate with the investigation, the husband still insisted that he would rather be fined than reveal anything. With failure in communication with the husband, and despite the health authorities having searched for the name of the company through multiple sources, the investigation was at a standstill. Fortunately, the Health Bureau of Tainan City revealed that before Japanese encephalitis was reported, the case was reported as influenza severe case, and at that time her husband mentioned that she had spent the night at her friend's house in Madou Township every Friday and Saturday for work before falling ill. And then the husband would not offer the address until he got the permission of the friend in Madou Township. After the health organization went to visit the friend in Madou Township and investigated, we finally knew the name of the temple that the case worked at, when and how the case went to work, and some parts of the progression and medical history, thus the investigation could continue further. We went to the temple for environment investigation and staff health inquiry, and we got the information that the case was a devout Buddhist and she made pilgrimages and did voluntary work often. In the end, we inquired the husband again, and he revealed that the case has attended 3 to 4 nights of spirit lectures during mid April to early May at a Buddha hall in Anping District, Tainan City. Therefore, the activity areas during the period of communicability of the case were 4 places, following by her house in Mid-western District, Tainan City; a Buddha hall in Anping District, Tainan City; the house of a friend in Madou Township, Tainan County; and workplace in a temple in Shiaying Township, Tainan County.

D. Activity areas (including her house) during the period of communicability, environmental investigation and the suspected infection origins: Activity areas of the case during the period of communicability and results from the environmental investigation are shown in Table 1. According to the results of the environmental investigation, the suspected infection origin was her workplace in Shiaying Township, Tainan County.

Table 1. Activity areas of the first case during the period of communicability and environmental investigation results

Activity area	Environmental investigation	Infection Origin
House in Mid-western District, Tainan City	Most were houses nearby, and close to the city, no adjacent paddy field, pigsty, aviary etc.	Excluded
A Buddha hall in section, Anping District, Tainan City	Across the Tainan City Hall, all neighborhoods were houses, and close to the city, no adjacent paddy field, pigsty, aviary etc.	Excluded
House of friend in Madou Township, Tainan County	Most were fruit farms nearby, 80 meters away from the house of friend has one resident family that kept 10 more chickens, and 400 meters away has a dove cottage, no paddy field or water reservoir like ponds.	Excluded
Work place in Shiaying Township, Tainan County	Most were dry farmland, vegetable field, and discarded pigsty nearby, there were some clear drains along the road (in which wrigglers of *Culex* species were found), about 100 meters behind the temple the case work at has a dove cottage, and there were some pigsties about 400 meters away, where hundreds of pigs were raised, and there was a big drainage ditch near the pigsty. Mosquito lamps were hung between 2 pigsties (3 places in total), 2 lamps were hung at the pigsty that was closest to the Buddha hall, and the other lamp was hung at other pigsties. In total, 27 *Culex tritaeniorhynchus* were caught, only one place was JEV positive.	Suspected

E. Results of Mosquito monitoring and JEV test by hanging the mosquito lamps around the suspected infection origins:

Because the case's workplace in Shiaying Township was the suspected infection origin, health workers hung mosquito lamps at 3 places near the pigsty to catch the vectors, thus strengthening the prevention measures and serving to confirm if there was any mosquito carrying JEV. The results of mosquito identification and JEV test were showed in Table 2, and it was proved that JEV-carrying mosquitoes were at the workplace in Shiaying Township. Combined with the activity condition of the case, environment investigation, and the results of mosquito monitoring and virus test, we hypothesized that the case was infected with Japanese encephalitis at her workplace in Shiaying Township.

Analysis of 8 Japanese encephalitis confirmed cases in southern district in 2010

From 2007 to 2009, the number of Japanese encephalitis confirmed cases in southern district from May to July were 6, 5, 0 cases, respectively. The total number of confirmed cases in southern district from May to July in 2010 was 8, which was more than the number recorded in any of the past 3 years. The first case in southern district in 2010 occurred in late May, and the other 7 cases all occurred in June (Table 3), which was more than epidemic threshold in southern district at the same period (4.0 cases). With the investigation of the 8 cases, we found that all of them had no record of receiving the Japanese encephalitis vaccine. Also, according to the results of environment investigation (Table 4.), risk factors for Japanese encephalitis infection did exist in both the residential area and the environment around the activity area of the cases. Environmental risk factors were most common in drains (100%) and dove cottages (100%), followed by paddy fields (87.5%), pigsties (37.5%), aviaries (37.5%), and animal farms (37.5%).

Table 2. The results of Mosquito identification and JEV test of the pigsties around the working area of the case in Shiaying Township, Tainan County

Lamp Code	A1	A2	B
Numbers of *Culex tritaeniorhynchus*	22	2	3
JEV	PCR positive	Negative	negative

Table 3. Number of Japanese encephalitis confirmed cases in south Taiwan from May to July, 2007-2010

	2007	2008	2009	2010
May	2	1	0	1
June	2	4	0	7
July	2	0	0	0
Total	6	5	0	8

Table 4. Environment risk factors of 8 Japanese Encephalitis confirmed cases in southern district in 2010.

Case	Reporting date	Age	Resident place	Environment investigation of highly suspected infection place (Environment risk factors in range of 1 meter circumference)	Result of mosquito monitoring 【lamp hanging location / whether *Culex tritaeniorhynchus* was caught or not / JEV test result】
Case 1	May 24th	50	Mid-western section Tainan City	Working area in Shiaying Township, Tainan County: Most were vegetable fields, there were some clear drains along the road (wrigglers of *Culex* species were found), 1 dove cottage, some pigsties, there was a big drainage ditch near the pigsty.	Pigsty / Yes (27 mosquitoes) / Positive
Case 2	June 7th	48	Shuilin Township Yunlin County	1. Around the house in Shuilin Township, Yunlin County: Paddy fields, drains near paddy fields (wrigglers of *Culex* species were found), chicken farms, goose farms, 1 dove cottage.	House / Yes (3 mosquitoes) / Negative
				2. A Buddha hall in Lioujiao Township, Chiayi County: Around the paddy fields (wrigglers of *Culex* species were found), 7 dove cottages.	Buddha hall / Yes (82 mosquitoes) / Negative
Case 3	June 11th	55	Shinshih Township Tainan County	Near the house in Shinshih Township, Tainan County: many paddy fields, 2 dove cottages, water reservoir at lawn (wrigglers of *Culex* species were found), drains.	No lamp
Case 4	June 15th	54	Shigang Township Tainan County	Near the house in Shigang Township, Tainan County: vegetable fields, fields (less water), drains, pigsties, 3 dove cottages.	No lamp
Case 5	June 25th	83	Chuchi Township Chiayi County	Near the house in Chuchi Township, Chiayi County: many paddy fields, drains, 2 dove cottages, chicken farms, goose farms, duck farms, a neighborhood raising large birds, the house without screen window.	No lamp
Case 6	June 28th	33	Puzih City Chiayi County	Near the house in Puzih City, Chiayi County: many paddy fields, drains (wrigglers of *Culex* species were found), 5 dove cottages, place that raised birds, chicken, goose, dogs, and sheep.	House / Yes (30 mosquitoes) / Negative
Case 7	June 30th	54	Jiali Township Tainan County	Near the house in Jiali Township, Tainan County: vegetable fields, fields (less water), open ground with many weeds, drains (less water), 7 dove cottages, place that raised birds, dogs and cows.	No lamp
Case 8	July 9th	38	Douliou City Yunlin County	1. Dorm of factory in Douliou City, Yunlin County: fruit farms, dry fields with many weed (with drains nearby) could retain some water when irrigation; there were 3 dove cottages and a space for raising birds, sheep, and dogs in the woods behind the dorm.	Sheepfold / Yes (3 mosquitoes) / Negative
				2. Wild birds shooting area in new industrial district in Douliou City, Yunlin County: many woods nearby, there were a lot of birds, 1 reservoir (with wrigglers of *Culex* species), one huge drain, one large pigsty with paddy fields around.	Pigsty / Yes (1155 mosquitoes) / Negative

Discussion and suggestions

Concerning the Japanese encephalitis confirmed cases, we have some suggestions for prevention measures based on the communicable diseases prevention working manual:

A. Epidemiological and environmental investigation: When health organizations reported Japanese encephalitis cases or investigated confirmed cases, cases were normally under poor health condition or even unconscious, and as a result, all information about progression of the illness, medical history, and activity area during the period of communicability was understood indirectly through the statements of family, friends, and neighbors. However, those people were not fully aware of the disease history, medical history, and activity situation of the case. Take Case 1 for example: the family refused to disclose the working location due to some personal reason, which stalled the investigation. In this situation, the health authorities should have worked on communicating with family and friends, while simultaneously gathering more information through previous disease reports, if they exist. As for environmental investigation, if any mosquito breeding grounds and animal or bird raising fields were found, personnel should take down the address and take photos immediately to record the relative distance and environmental situation. Also, among lamps that hung at the cases' houses or activity areas, vector mosquitoes were caught in 6 places only, and only the lamp hung at the pigsty near the first case's workplace caught mosquitoes that carried the virus on May 28; other lamps were hung after mid June. Although *Culex tritaeniorhynchus* were caught, but there was no virus found, maybe because the virus' active season was in May [5]. Further discussion is needed to identify other potential explanations.

B. Preventive inoculation: The most effective way to prevent Japanese encephalitis is inoculation, and the Japanese encephalitis inoculation schedule for children in Taiwan is from March through May every year. We suggest that the local health authorities step up their effort to push for Japanese encephalitis inoculation during the season in which the disease is prevalent. After a confirmed case appears, while proceeding with epidemic investigation around the case's activity area (including house), the inoculation status of the family members who lived with case and residents around the case should be checked. Children of the right age who have not been inoculated should get the vaccine as soon as possible. Additionally, adults can get vaccination at their own cost if needed.

C. Health education promotion and health monitoring: Local health authorities should strengthen health education about Japanese encephalitis prevention and treatment to family members who lived with cases and residents around the suspected infection origin (including house). During the prevalent season of Japanese encephalitis, we can remind people about mosquito prevention measures and inoculation information via media channels like press releases, radio broadcasts, and posters. Finally, it is advisable to implement health monitoring on population groups who were apt to have more evident clinical signs after being infected (e.g. elderly people and children) and who lived around the suspected infection origins.

D. Implement disease monitoring, visit medical care institutions, and enhance the reporting system.

E. Hanging mosquito lamps: After being evaluated by the CDC and consulting specialists, considering the unfavorable outcomes of chemical prevention measures (i.e. insecticide spray) on Japanese encephalitis, we suggest adding into the Japanese encephalitis prevention and treatment manual the following instruction: "After an epidemic investigation, mosquito lamps can be used to catch the vectors by hanging them over possible locations where the case was infected and places with high risk (e.g. livestock farms)." Furthermore, the government should offer mosquito lamps to local health authorities for hanging at areas where Japanese encephalitis cases were suspected to have caught their disease, in order to catch the virus-carrying vectors and to decrease the density of those vectors. Additionally, through the present investigation, we found that we could get further information and confirmation about infection sources of Japanese encephalitis by using mosquito lamps, which is worth further evaluation and research.

Acknowledgment

We would like to thank the investigation and testing center of CDC for the mosquito identification and virus examination, and fellow workers at Tainan City, Tainan County, Chiayi County, the Health Bureau and station of Yunlin County for epidemic investigation and cooperation of hanging the mosquito lamps.

References

1. David W. Vaughn and Charles H. Hoke, Jr. The epidemiology of Japanese encephalitis: prospects for prevention. Epidemiol Rev 1992;14;197-221.
2. Solomon T, Dung NM, Kneen R, et al. Japanese encephalitis. J Neurol Neurosurg Psychiatry 2000;68:405-15.
3. Wu YC, Huang YS, Chien LJ,_et al. The epidemiology of Japanese encephalitis on Taiwan during 1966–1997.Am J Trop Med Hyg 1999;61:78-84.
4. Taiwan CDC. Disease introduction – Japanese encephalitis. Available at:http://www.cdc.gov.tw/sp.asp?xdurl=disease/disease_detail.asp&id=778&mp=1&ctnode=1498
5. Lin C, Jian SW, Teng HJ. Surveys on Japanese encephalitis vectors in Taiwan area during 2004-2008. Taiwan Epidemiology Bulletin.2010;26:158-65.

Biosafety and Biosecurity

Policy to Recommend the Identification of *M. Tuberculosis* and Drug Susceptibility Test in Biosafety Level 3 Laboratory

Yu-Yen Shih, Wen-Chao Wu, Jer-Jea Yan

Fifth Division, Centers for Disease Control, Taiwan

The World Health Organization (WHO) has estimated that the annual incidence of tuberculosis (TB) is around 1/1000. Overall, 2 billion people, approximately one-third of the world's population is currently infected with *M. tuberculosis*. The largest number of TB cases occurred in the South-East Asia Region and China [1-2]. In 2008, there were 14,265 confirmed TB cases in Taiwan, and the incidence was 62/100,000 populations. There was a 14% reduction in incidence rate of tuberculosis from 2005 to 2008. To be in accordance with the strategy of "The Global Plan To Stop TB 2006-2015" launched by WHO, our goal is to halve tuberculosis prevalence and death rates in ten years. Nevertheless, ensuring the quality of protection and safety for laboratory personnel during the execution of the strategy is the concern of the government as well [3].

Mycobacterium tuberculosis (referred to as tuberculosis) belongs to a risk group 3 (RG3) pathogen, and it has high risk of infection for laboratory technicians. To ensure the safety and effectiveness of laboratory practices, the activities about cultures of tuberculosis and drug susceptibility test (referred to as susceptibility test) should be carried out under biosafety level 2 (BSL-2) containments in negative pressure system with BSL-3 safety equipment and work practices by decree of Taiwan Centers for Disease Control (TCDC). However, the regulations should be timely assessed and the biosafety level can be elevated if needed.

Recent studies indicate that the risk of tuberculosis infection in people working in tuberculosis laboratories is three to nine times higher than the risk of other laboratorians [4]. Furthermore, the risk of infection varies in different laboratory techniques (microscopy: culture: susceptibility test: staff not working in laboratories =1.4:1.9:21.5:1) [5]. In addition, WHO, the developed countries in Europe and America (such as Belgium, Canada, and the United States) and in Asia (e.g., China, Japan and Singapore) all recommended that procedures involving identification of tuberculosis and antimicrobial susceptibility testing are to be performed in BSL-3 facilities [4, 6-8]. In Taiwan, the identification of tuberculosis and susceptibility test had been carried out under biosafety level 2 (BSL-2) containments with negative pressure system since 2008 considering the target to halve tuberculosis in ten years and the facilities and resources of laboratories. However, after reviewing the laboratory work in the past years, the importance of biosafety and how to connect with international standards is well acknowledged by the authorities. To make policy changes for the contained use of tuberculosis is well justified.

Considering many factors such as the resources for halving tuberculosis in ten years, the time and cost of constructing a BSL-3 laboratory (consists of double-door autoclave, 24-hour exhaust air ventilation system, and backup ventilation system), as well as the deliberation regulations of laboratories [9], it is estimated that approximately 18 months to 2 years will be needed from developing to start using the new BSL-3 tuberculosis laboratory. Therefore, medical institutes are encouraged to upgrade their tuberculosis laboratories to BSL-3 laboratories or installation of new BSL-3 laboratory before 2014 and obtain approval from TCDC. From 2012, annual evaluation of the capability and caseload of identification of tuberculosis and drug susceptibility test in BSL-3 laboratory will be reviewed. If BSL-3 laboratories achieve the target, the regulation will be enforced to implement this policy with the purpose of ensuring the safety of laboratory technicians and connecting with international standards.

References

1. WHO. Tuberculosis. Available at: http://www.who.int/mediacentre/factsheets/fs104/en/
2. WHO. Global TB database. Available at: http://www.who.int/tb/country/global_tb_database/en/index.html
3. Taiwan CDC. Halving tuberculosis in ten years: Phase two. 2010.Available at: http://www.cdc.gov.tw/ct.asp?xItem=5658&CtNode=1517&mp=230
4. Philippe H, Maryse FD, Didier B, et al ,Biosafety Recommendations for the Contained Use of Mycobacterium tuberculosis Complex Isolates in Industrialized Countries. Division of Biosafety and Biotechnology 2006.
5. Kim SJ, Lee SH, Kim IS, et al. Risk of occupational tuberculosis in National Tuberculosis Programme laboratories in Korea. Int J Tuberc Lung Dis 2007;11(2):138-42.
6. WHO. Policy guidance on drug-susceptibility testing (DST) of second-line antituberculosis drugs. Available at: http://www.who.int/tb/publications/2008/whohtmtb_2008_392/en/index.html
7. Health Canada. Guidelines for preventing the transmission of tuberculosis un Canadian health care facilities and other institutional settings. CCDR 1996;22S1.
8. CDC. Interim Laboratory Biosafety Guidance for Extensively Drug-Resistant (XDR) Mycobacterium Tuberculosis strains. Available at: http://www.cdc.gov/tb/topic/laboratory/BiosafetyGuidance_xdrtb.htm
9. Taiwan CDC. Regulations governing management of infectious biological materials and collection of specimens from patients of communicable diseases. 2005 Available at:http://www.cdc.gov.tw/ct.asp?xItem=2740&ctNode=1604&mp=1

Introduction of Laboratory Biosafety Regulations in the United States

Chih-Heng Liao

Department of Laboratory Accreditation, Taiwan Accreditation Foundation

Bioterrorism was recognized as a serious problem after September 11 attacks in 2001 and the subsequent anthrax mail threat in the United States. In response, the Congress and the Federal Government authorities reinforced the examination process on biological hazardous materials. Strict legislations were also made to regulate the transport, management and use of the pathogenic materials.

To prevent the spread of terrorism, the Antiterrorism and Effective Death Penalty Act of 1996 was signed by the United States Congress. Countries supporting terrorism would face prosecution and obtaining financial resources from America would become more difficult. The immigration laws were revised to take precautions against terrorists' infiltration into the United States. From the perspective of biosafety, the antiterrorism act has authorized the Department of Health and Human Services (HHS) to make and enact laws to list and regulate the potential biological hazardous materials that pose a threat to public health and safety; standard operating procedures on transport and control measures should be made to prevent non-authorized obtainment and to assure a legitimate use of these pathogenic materials for research, teaching, and so on. HHS has entrusted Centers for Disease Control and Prevention (CDC) to issue the associated stipulations into Title 42 Part 72 of the Code of Federal Regulations. Therefore, CDC listed the select agents, including more than 30 kinds of viruses, bacteria, rickettsiae, fungi, and toxins; regulations governing institutions that transport or deposit biological hazardous material or institutions classified as biosafety level (BSL) 2 to BSL 4 on the requests, registration, verification of registration, transfer, disposal, exemptions, and penalties were made.

In addition to the laws regulate the interstate transportation made by CDC, the other government authorities also issued rules on transportation of potential hazardous material. For example, the Department of Transportation (DOT) has specified the classification and package rules on intrastate, interstate, and international transportation of hazardous material in Title 49 Parts 171-180 of the Hazardous Material Regulations (HMR). The International Civil Aviation Organization (ICAO) also made the Technical Instructions for the Safe Transport of Dangerous Goods by Air according to the United Nation's recommendations. Some ICAO standards and regulations regarding the air transportation are adopted by the Department of Transportation.

Pathogens, hosts, and transmission vectors, such as mosquitoes, ticks, and snails, are frequently imported into the United States for research, but importation of pathogenic material, arthropods, hosts or transmission vectors of human diseases is not allowed unless it is authorized by CDC according to

Title 42 Part 71.54 of the Code of Federal Regulations. Authorized importers should pack, mark, and transport according to the laws after authorization; the importers should offer certification of the shipping company. Department of Agriculture also addressed that organisms and vectors are not allowed to import to the United States in Title 9 Part 122 of the Code of Federal Regulations. The Animal and Plant Health Inspection Service (APHIS) listed the regulated articles imported from other countries, transported between states, or released into the environment in Title 7 Part 340 of the Code of Federal Regulations, including donor organism or recipient of material potentially hazardous to animals or plants, vectors, vector agents, and genetically modified organisms. Interstate transport and import are legitimate under strict regulations. The first application shall be submitted 60 days prior to transport and multiple items can be applied in combination.

Regulations associated with laboratory biosafety used currently are listed as following:

1. Biosafety in the Microbiological and Biomedical Laboratories (BMBL) published by US CDC:

   Standard operating procedures in microbiological laboratories, laboratory design, standard biosafety equipments, and details about BSL1 to BSL 4 laboratories are described. For programmatic implementation, microbes are classified into 4 risk groups (RG) based on their potential to damage human health. The 5th edition was published in 2009.

2. Guidelines for Research Involving Recombinant DNA Molecules published by National Institutes of Health (NIH):

   Operating guidelines about researches involving recombinant DNA molecules and organisms/viruses containing recombinant DNA molecules are established and all researches involving recombinant DNA are included. Study subjects are divided into 3 groups (microbes, animals, and plants) and laboratories are divided into general laboratory and laboratory that deals with large-scale culture. No matter what research the laboratory is doing, the classification of BSL, standard operating procedures, and biosafety protection level should be consistent with BMBL. The risks of researches involving biosafety issues should be assessed by an institutional biosafety committee or biosafety officer. Researches can be initiated only after adequate biosafety precautions and protection have been made. The guidelines have been partially revised in 2011.

3. Occupational Safety and Health Act issued by Occupational Safety and Health Administration (OSHA):

   The Act was first enacted in 1970 to improve occupational safety and health. Bloodborne Pathogens Standard, Standard for Exposure to Hazardous Chemicals in Laboratories, Hazard Communication Standard, Hazardous Waste Operating and Emergency Response Standard, Standards for Personal Protective Equipment, Standards Regarding Medical Services and First Aid, Air Contaminants Standard, and Standards Applicable to Specific Hazardous Materials were issued accordingly.

References

1. Biotechnology Industry Organization. Laboratory biosafety issues, BIO Safety and Security Committee. 2002. Available at: http://www.umbc.edu/safety/Laboratory%20BioSafetyFinal.pdf
2. CDC. Biosafety in the Microbiological and Biomedical Laboratories 5th ed, 2009. Available at: http://www.cdc.gov/biosafety/publications/bmbl5/BMBL.pdf