Evaluating the importation of yellow fever cases into China in 2016 and strategies used to prevent and control the spread of the disease

Chao Li
Public Health Emergency Center, Chinese Center for Disease Control and Prevention

Dan Li
Public Health Emergency Center, Chinese Center for Disease Control and Prevention

Shirley JoAnn Smart
Georgia Southern University, Jiann-Ping Hsu College of Public Health

Lei Zhou
Public Health Emergency Center, Chinese Center for Disease Control and Prevention

Peng Yang
Beijing Center for Disease Control and Prevention

Follow this and additional works at: https://digitalcommons.georgiasouthern.edu/bee-facpubs

Part of the Biostatistics Commons, and the Epidemiology Commons

See next page for additional authors

Recommended Citation
Li, Chao, Dan Li, Shirley JoAnn Smart, Lei Zhou, Peng Yang, Jianming Ou, Yi He, Ruiqi Ren, Tao Ma, Nijuan Xiang, Haitian Sui, Yali Wang, Jian Zhao, Chaonan Wang, Yeping Wang, Daxin Ni, Isaac Chun-Hai Fung, Dexin Li, Yangmu Huang, Qun Li. 2020. "Evaluating the importation of yellow fever cases into China in 2016 and strategies used to prevent and control the spread of the disease." Western Pacific Surveillance and Response, 11 (2): 1-6: World Health Organization (WHO). doi: https://doi.org/10.5365/wpsar.v11i2.606
source: https://doi.org/10.5365/wpsar.v11i2.606
https://digitalcommons.georgiasouthern.edu/bee-facpubs/188

This article is brought to you for free and open access by the Biostatistics, Epidemiology, and Environmental Health Sciences, Department of at Digital Commons@Georgia Southern. It has been accepted for inclusion in Biostatistics, Epidemiology, and Environmental Health Sciences Faculty Publications by an authorized administrator of Digital Commons@Georgia Southern. For more information, please contact digitalcommons@georgiasouthern.edu.
During the yellow fever epidemic in Angola in 2016, cases of yellow fever were reported in China for the first time. The 11 cases, all Chinese nationals returning from Angola, were identified in March and April 2016, one to two weeks after the peak of the Angolan epidemic. One patient died; the other 10 cases recovered after treatment. This paper reviews the epidemiological characteristics of the 11 yellow fever cases imported into China. It examines case detection and disease control and surveillance, and presents recommendations for further action to prevent additional importation of yellow fever into China.

The 2016 yellow fever outbreak in Angola led to renewed attention to this often-fatal disease. Of the 4306 suspected cases reported, 376 individuals died (mortality rate, 8.7%). The outbreak was declared to have been one of the largest and most challenging yellow fever outbreaks in recent years by the World Health Organization (WHO), in part because of its international spread to other countries, including China.

Yellow fever is a zoonotic disease that is endemic in tropical regions of Africa and South America. It is caused by the yellow fever virus, an arbovirus that belongs to the *Flavivirus* genus. The virus is transmitted between humans, or from monkeys to humans, through the bite of infected mosquitoes belonging to the *Aedes* and *Haemagogus* genera, respectively. Yellow fever causes an estimated 30 000 deaths each year, most of which are in Africa, where more than 500 million people are at risk for yellow fever. An additional 400 million people in Central and South America are also at risk. Though *Aedes aegypti* mosquitoes are found in China (primarily in Fujian Province) and other parts of Asia, yellow fever had never, before 2016, been reported in China or any other part of Asia.

In 2015, more than 200 000 Chinese nationals were working or conducting business in Angola. According to the General Administration of Quality Supervision, Inspection and Quarantine (AQSIQ), dozens of the Chinese nationals in Angola contracted yellow fever during the 2016 outbreak, resulting in eight deaths in Angola. Facing the possibility of an imported yellow fever epidemic, China developed a national yellow fever control and prevention protocol, and took steps to strengthen surveillance at airports and health-care facilities and to implement emergency vector surveillance. Despite these efforts, 11 Chinese nationals who were infected during the outbreak in Angola imported yellow fever into China in 2016.
Considering frequent travel, labour relationships, and close trade with endemic countries in South America and Africa, China faces a continued risk of yellow fever importation. Therefore, the purpose of this paper is to examine China’s response to the importation of its first yellow fever cases, particularly the emergency response, as well as case detection and disease surveillance and control.

METHODS

We obtained and analysed data collected as part of China’s emergency response. The following paragraphs describe the steps taken to identify and document the imported cases of yellow fever and to collect demographic and epidemiological data, as well as clinical information.

Case definition

Suspected cases of yellow fever were identified by clinicians based on clinical manifestations consistent with yellow fever, which included fever, jaundice, liver and kidney dysfunction, vomiting, and bleeding, as well as epidemiological history (i.e. history of travel or residence in the last 14 days before symptom onset). Confirmed cases were defined as suspected cases that tested positive for yellow fever virus using nucleic acid testing.6

Data collection

Once a suspected case was diagnosed by a laboratory, the provincial CDC conducted a field investigation to collect demographic and epidemiological information (including travel history, i.e. the dates of arrival in Angola and return to China and yellow fever vaccination status) and clinical information (including symptoms, time of symptom onset and date of hospital visit).

Vector surveillance

Routine surveillance of *Aedes* density has been conducted in China for many years. According to the surveillance protocol,9 all provinces are classified into three groups (high, middle and low) depending on the level of risk of mosquito-borne disease transmission. In high-risk areas, surveillance is conducted throughout the year. In middle- and low-risk areas, surveillance is conducted from May to November and from June to September. After each of the imported cases of yellow fever was identified, emergency monitoring was conducted to measure the mosquito density within a radius of 200 metres of the patient’s residence. The Breteau Index (BI) was calculated to determine the number of positive containers per 100 households inspected.9

Ethics approval and consent to participate

The case information was collected according to the regulations of the Law of the People’s Republic of China on the Prevention and Treatment of Infectious Diseases as a part of the emergency response, which was exempted from ethics approval and consent to participate.

RESULTS

Case characteristics

A total of 11 cases of yellow fever were reported in China, all imported from Angola. All were Chinese nationals living in Luanda, the capital of Angola, at the time of the outbreak. Seven cases were residents of Fujian Province, two of Jiangsu Province, and one each of Zhejiang Province and Sichuan Province. All cases were identified in weeks 11 to 15 of 2016, approximately one to two weeks after the peak of the Angolan epidemic. The patient age range was 18–52 years (median: 42 years). Eight were male, and three were female. Eight were retailers, and
Evaluating the importation of yellow fever cases into China

Li et al

Disease control and surveillance

The Chinese Government took steps to strengthen surveillance at airports and health-care facilities and implemented emergency vector surveillance in an attempt to prevent further cases of yellow fever. Specifically, the Government intensified multisectoral coordination and collaboration; strengthened surveillance, vector monitoring and risk assessment; enhanced clinical management of yellow fever cases; conducted vector control activities; carried out public risk communication activities; and deployed a medical team to Angola to provide yellow fever vaccination to unvaccinated Chinese nationals.

DISCUSSION

We describe the 11 cases of imported yellow fever in China, most of which were discovered within two weeks after the peak of the outbreak in Angola in 2016. After the outbreak in Angola was announced, China quickly released a protocol for yellow fever prevention and control. At the same time, AQSIQ, in the hope of preventing

Table 1. Demographic characteristics of imported cases of yellow fever

| Case no. | Sex | Age (years) | Date of symptom onset | Reporting region | Location at time of diagnosis | Vaccination status | Reporting institution | Notes | Data source |
|----------|-----|-------------|-----------------------|------------------|------------------------------|-------------------|----------------------|-------|-------------|
| 1        | M   | 32          | 8 March 2016          | Beijing          | Beijing                      | Not vaccinated before symptom onset | AQSIQ               | Died of the disease  | 10,19–21 |
| 2        | M   | 46          | 5 March 2016          | Shanghai         | Shanghai                     | Unknown            | AQSIQ               |                   | 22      |
| 3        | M   | 44          | 9 March 2016          | Beijing          | Beijing                      | Not vaccinated before travel to Angola | AQSIQ               |                   | 10,23   |
| 4        | M   | 44          | 11 March 2016         | Beijing          | Beijing                      | Not vaccinated before travel to Angola | AQSIQ               |                   | 10,23   |
| 5        | M   | 50          | 6 March 2016          | Beijing          | Beijing                      | Not vaccinated before travel to Angola | AQSIQ               | Received treatments in multiple hospitals in Angola from 6 to 16 March 2016 | 10,24   |
| 6        | F   | 42          | 11 March 2016         | Fujian           | Fuzhou                       | Not vaccinated before travel to Angola. Vaccinated in Angola on 7 March 2016, 3 days before symptom onset. | Medical Institution |                   | 10,25   |
| 7        | M   | 42          | 17 March 2016         | Fujian           | Fuzhou                       | Vaccinated 7 days before symptom onset | Medical Institution |                   | 10,26   |
| 8        | F   | 36          | 15 March 2016         | Fujian           | Fuzhou                       | Vaccinated 5 days before symptom onset | Medical Institution |                   | 10,26   |
| 9        | F   | 53          | 13 March 2016         | Fujian           | Fuzhou                       | Vaccinated 1 day before symptom onset | Medical Institution |                   | 10,26   |
| 10       | M   | 18          | 12 March 2016         | Fujian           | Fuzhou                       | Vaccinated 10 days before symptom onset | Medical Institution |                   | 10,27   |
| 11       | M   | 29          | 5 April 2016          | Beijing          | Beijing                      | Vaccinated 10 months before symptom onset | AQSIQ               | Sought medical care at a local hospital in Angola | 10,11   |

AQSIQ, General Administration of Quality Supervision, Inspection and Quarantine.
yellow fever from entering China, issued an announce-
ment that included instructions for screening travellers
and checking vaccination certificates.\textsuperscript{12}

Several strategies were implemented to control
the spread of yellow fever in China. First, all travellers
from Angola were required to present yellow fever vac-
cination certificates. Those without a certificate were
isolated at the point of entry or their place of residence
for six days. Second, all travellers from affected countries
were screened upon entry. Anyone who self-declared or
who was suspected of having yellow fever was isolated
at the entry point. There, AQSIQ staff administered an
epidemiological survey and collected blood samples for
testing. Third, travellers from Angola and other epidemic
countries were required to perform self-health monitoring
for six days after entering China. If suspicious symptoms
occurred, the affected traveller was asked to report to a
health-care provider, disclose their travel history and
receive prompt treatment. Additionally, aircraft, contain-
ers and other cargo from the epidemic countries were
targeted for mosquito control. It was also recommended
that persons travelling to Angola and other epidemic
countries should be vaccinated again for yellow fever be-
fore departure from China. For the imported yellow fever
cases, emergent monitoring of mosquito-borne vectors
was also performed.

Areas recommended for improvement include
epidemic information sharing, risk warning and health
education for Chinese nationals in Angola and other yel-
low fever-endemic countries. According to our investiga-
tion, Chinese nationals in Angola are generally employees
sent by private companies or individual business people,
primarily from Fuqing City in Fujian Province. More
than 200 000 Chinese nationals live and work outside
China,\textsuperscript{3} so timely health-related communication between
health officials, companies and overseas workers could
help protect China's expatriate population from public
health threats in their countries of temporary residence.
Overseas workers in Angola should have received a yel-
low fever vaccination before their departure from China.
Information about the yellow fever epidemic, if received
from their companies or Chinese health officials, might
have encouraged personal prevention measures such as
mosquito-avoidance precautions. Information on travel-
ers with yellow fever, especially those who returned to
China for treatment, should have been reported by the
employing companies to the Chinese embassy or Govern-
ment, which would have provided valuable information
for disease prevention. Required vaccination and im-
poved communication are also crucial for individual busi-
ness people who are travelling to yellow fever-endemic
countries. All inbound passengers should be required to
present proof of vaccination if they are arriving from yel-
low fever-endemic countries. Health education materials
e.g. videos, posters, warning signs, brochures and text
messages) could be provided at the points of entry by
inspection and quarantine officials to encourage inbound
passengers to self-declare symptoms of a potential com-
municable disease.\textsuperscript{13}

Additional strategies have been identified and are
recommended for reducing the risk of importation and
spread of infectious diseases in China. For instance,
China could strengthen regulations and legislation to put
an end to the fabrication of false yellow fever vaccination
certificates, a practice used to circumvent the vaccina-
tion regulations of the International Health Regulations,
or IHR (2005). Globally, governments, including that of
China, could ensure their citizens receive yellow fever
vaccination when travelling to countries that recommend
it, could tighten border controls to ensure incoming
visitors from yellow fever-endemic countries have proof
of vaccination and could make public policies a priority in
the prevention of diseases among travellers.\textsuperscript{14}

The active period for the \textit{Aedes aegypti} mosquito in
Fujian Province was reported to be from May to October
in 2016.\textsuperscript{15} However, the result of emergency monitor-
ing (BI: 15) indicated continued transmission risk of
mosquito-borne diseases after the peak period. Thus, the
public should be educated to eliminate containers that
can hold water in which mosquitoes may breed.

\textbf{Risk of disease importation}

Due to frequent travel and close trade with yellow fever-
endemic countries in Africa and South America, China
faces a continued risk of yellow fever importation as travel
volume has increased. Travel patterns to and from yellow
fever-endemic regions in relation to China indicate that
Angola sends the second-highest number of travellers into
China and also receives the second-highest number of
Chinese visitors.\textsuperscript{14} During the years 2010–2030, tourist
arrivals in Asia and the Pacific are expected to increase
by 331 million, bringing the total number of tourists to
about 535 million in 2030. With this increase in travel,
there will be a concomitant increase in the importation of infectious diseases. Due to the presence of the urban mosquito vector, *Aedes aegypti*, among large unvaccinated populations, 1.8 billion people in Asia were put at risk for yellow fever by international travellers during the 2016 outbreak. In Angola, by September 2016, near the end of the 2016 yellow fever outbreak, 884 laboratory-confirmed cases of yellow fever had been reported, with 373 deaths. The confirmed cases of yellow fever in China were the first-ever cases to be imported into Asia.

In 2012, a total of 475,761 air passengers travelled to China from yellow fever-endemic countries. Of those, 195,291 travelled from the South American countries of Argentina, Brazil, Columbia and Venezuela, and 104,854 travelled from the African countries of Angola, Ethiopia, Ghana and Nigeria. During that same year, 466,832 air passengers from China travelled to yellow fever-endemic countries. The importation of yellow fever from endemic countries by unvaccinated Chinese workers is a serious concern, as they are apparently able to circumvent the mandated IHR (2005) regulations that require proof of vaccination for entry into China from certain yellow fever-endemic countries, including Angola.

**Vaccinations**

Finally, although yellow fever is a vaccine-preventable disease, the vaccination rate of yellow fever in Chinese nationals in Angola is estimated to be very low. Vaccinations should be required for all Chinese nationals going to or returning from countries where yellow fever is endemic, as per the WHO recommendations. This would protect Chinese citizens who are residing in countries such as Angola and Brazil, where the risk of contracting yellow fever is substantial.

The WHO risk assessment report of yellow fever infection in non-immunized travellers underlined the need to reinforce the implementation of yellow fever vaccination requirements and highlighted the risk of international spread of the disease through non-immunized travellers. A safe and effective vaccine for yellow fever has been available for more than 50 years. The licensed, live attenuated yellow fever vaccine produces immunization within 10 days and has a long duration of immunity. However, it is in short supply, with only about 80 million doses produced annually. An estimated half a million doses of the vaccine would be needed annually to cover the Chinese population travelling to yellow fever-endemic countries. Yellow fever 17D vaccine is manufactured in China for the domestic market and therefore is available, although the supply is limited.

Routine vaccination for children living in countries at risk for yellow fever is also recommended by WHO. The vaccine confers long-term protection (10 years or more, possibly lifelong) within 10 days for more than 90–95% of individuals who receive the vaccine. Within 30 days after vaccination, 99% of those immunized develop immunity. A single dose is likely to provide lifelong immunity. The yellow fever vaccination certificate is now valid for the duration of the life of the person vaccinated.

Among the 11 cases, there were two cases with vaccination failure. Although vaccination failure for yellow fever is unusual, some studies showed up to 26% seronegativity in vaccines after mass immunization campaigns. External factors such as improper cold chain handling, storage and administration may be the cause of failure.

In conclusion, we have described the first-ever importation of yellow fever cases in China, discussed the methods used for case detection and prevention of imported infectious disease, and provided several recommendations for disease prevention and control. Experiences gained from the response to imported yellow fever cases in 2016 can be used to protect Chinese travellers from yellow fever and to prevent new importations of the disease.

**Acknowledgements**

We would like to thank AQSIQ staff at the points of entry in Beijing and Shanghai and provincial CDC staff for assisting with data collection.

**Funding**

This work was supported by the World Bank Avian/Human Influenza Trust Fund Grant Project of Capacity Building for Emerging Infectious Diseases Control and Prevention in China (grant no. TF012401), the World Health Organization Project of Improvement of Surveillance System of Emerging Infectious Diseases in China (grant no. WPDSE1611306) and the World Health Organization Project of Assess Risks of Emerging Infectious Diseases in China (grant no. WPCIN1814401).
References

1. The yellow fever outbreak in Angola and Democratic Republic of Congo ends. Brazzaville: World Health Organization Regional Office for Africa; 2017. Available from: https://www.who.int/en/news-room/fact-sheets/detail/yellow-fever. Accessed 24 April 2017.

2. Shi P-Y, editor. Molecular virology and control of flaviviruses. Poole: Caister Academic Press; 2012.

3. Yellow fever fact sheet. Geneva: World Health Organization; 2016. Available from: https://www.who.int/en/news-room/fact-sheets/detail/yellow-fever. Accessed 24 April 2017.

4. Yang J, Zhou PC, Wang J. 质检部门与驻安哥拉使馆黄热病防控重要措施研究. (Research on the important measures for yellow fever prevention and control from the authority of IHR and the Embassy of Angola). Chinese Journal of Hygienic Insecticides & Equipments. 2017;23(1):82–7 (in Chinese).

5. 中国政府高度重视海外公民健康 派出工作组赶赴安哥拉紧急救助 (The Chinese government attaches great importance to the health of overseas citizens, and has dispatched a working group to rush to Angola for emergency relief). Beijing: General Administration of Quality Supervision, Inspection and Quarantine of the People's Republic of China; 2016 (in Chinese). Available from: http://www.cqn.com.cn/zj/content/2016-04/05/content_2675144.htm. Accessed 5 April 2018.

6. 关于印发黄热病防控方案 (2016年版) 的通知 (Protocol for prevention and control for yellow fever (2016 version)). Beijing: National Health and Family Planning Commission; 2016 (in Chinese). Available from: http://www.nhc.gov.cn/jk/s9260/s12879-018-201604/s12879-018-50020/s12879-018-50020-20160402/10153777.html. Accessed 22 April 2016.

7. Cui S, Pan Y, Liu Y, Liang Z, Li J, Sun Y, et al. Detection of yellow fever virus genomes from four imported cases in China. Emerg Infect Dis. 2017 Jul;24(7):1383–6. doi:10.3201/eid2407.171868 pmid:29723485

8. 黄热病防控方案(2016年版)的通知 (Protocol for prevention and control for yellow fever (2016 version)). Beijing: National Health and Family Planning Commission; 1989 (in Chinese). Available from: http://www.chinacdc.cn/kjdtkhwztb/200804/t18963.shtml. Accessed 21 March 2018.

9. 登革热病例监测指南 (Dengue fever control technical guidelines). Beijing: Chinese Center for Disease Control and Prevention; 2014 (in Chinese). Available from: http://www.chinacdc.cn/kjdtkhwztb/201004/t104958.html. Accessed 23 May 2018.

10. Song R, Guan S, Lee SS, Chen Z, Chen C, Han L, et al. Late or lack of vaccination linked to importation of yellow fever from Angola to China. Emerg Infect Dis. 2018 Jul;24(7):1383–6. doi:10.3201/eid2407.171868 pmid:29723485

11. Yellow fever - China. WHO Disease Outbreak News. 22 April 2016. Available from:https://www.who.int/ith/updates/20160727/en/

12. 中华人民共和国国境卫生检疫法实施细则 —— 新版 (Regulations on the Implementation of the Frontier Health and Quarantine Law of PRC). Beijing: National Health and Family Planning Commission; 1989 (in Chinese). Available from: http://www.nhc.gov.cn/jk/zcgljwjsj/200804/t85077.shtml. Accessed 21 March 2018.

13. New yellow fever vaccination requirements for travellers. World Health Organization. 27 July 2016. Available from: https://www.who.int/ith/updates/20160727/en/

14. Gotuzzo E, Yactayo S, Córdova E. Efficacy and duration of immunity after yellow fever vaccination: systematic review on the need for a booster every 10 years. Am J Trop Med Hyg. 2013 Sep;89(3):434–44. doi:10.4269/ajtmh.13-0264. pmid:24006295

15. Chen Z, Liu L, Li Y, Zhang W, Li J, Zhang Y, et al. A fatal yellow fever virus infection in China: description and lessons. Emerg Microbes Infect. 2016 Jun 13;5(1):1–8. doi:10.1038/emi.2016.89. pmid:27406389

16. Yellow fever - China. WHO Disease Outbreak News. 29 Mar 2016. Available from: https://www.who.int/ith/updates/20160329-2016-yellow-fever-china/en/. Accessed 3 November 2018.

17. 黄热病防控方案 (2016年版) 的通知 (Protocol for prevention and control for yellow fever (2016 version)). Beijing: National Health and Family Planning Commission; 2016. Available from: http://www.cqn.com.cn/zj/content/2016-03/14/content_5003385.htm. Accessed 23 March 2016.

18. Selvey LA, Antão C, Hall R. Entry screening for infectious diseases in humans. Emerg Infect Dis. 2015 Feb;21(2):197–201. doi:10.3201/eid2102.131610 pmid:25625224

19. Wilder-Smith A, Leong WY. Importation of yellow fever into China: assessing travel patterns. J Travel Med. 2017 Jul;24(4):tax008. doi:10.1193/htm/tax008 pmid:28426111

20. Cui S, Pan Y, Lyu Y, Liang Z, Li J, Sun Y, et al. Detection of yellow fever virus genomes from four imported cases in China. Int J Infect Dis. 2017 Jul;60:93–5. doi:10.1016/j.ijid.2017.05.001 pmid:28623054

21. 中华人民共和国国境卫生检疫法实施细则 —— 新版 (Regulations on the Implementation of the Frontier Health and Quarantine Law of PRC). Beijing: National Health and Family Planning Commission; 1989 (in Chinese). Available from: http://www.gov.cn/xinwen/2016-03/14/content_5053385.htm. Accessed 22 April 2016.

22. New yellow fever vaccination requirements for travellers. World Health Organization. 27 July 2016. Available from: https://www.who.int/ith/updates/20160727/en/

23. Gotuzzo E, Yactayo S, Córdova E. Efficacy and duration of immunity after yellow fever vaccination: systematic review on the need for a booster every 10 years. Am J Trop Med Hyg. 2013 Sep;89(3):434–44. doi:10.4269/ajtmh.13-0264. pmid:24006295

24. Selvey LA, Antão C, Hall R. Entry screening for infectious diseases in humans. Emerg Infect Dis. 2015 Feb;21(2):197–201. doi:10.3201/eid2102.131610 pmid:25625224

25. Wilder-Smith A, Leong WY. Importation of yellow fever into China: assessing travel patterns. J Travel Med. 2017 Jul;24(4):tax008. doi:10.1193/htm/tax008 pmid:28426111

26. Cui S, Pan Y, Lyu Y, Liang Z, Li J, Sun Y, et al. Detection of yellow fever virus genomes from four imported cases in China. Int J Infect Dis. 2017 Jul;60:93–5. doi:10.1016/j.ijid.2017.05.001 pmid:28623054

27. 中华人民共和国国境卫生检疫法实施细则 —— 新版 (Regulations on the Implementation of the Frontier Health and Quarantine Law of PRC). Beijing: National Health and Family Planning Commission; 1989 (in Chinese). Available from: http://www.gov.cn/xinwen/2016-03/14/content_5053385.htm. Accessed 22 April 2016.