



RAPID RISK ASSESSMENT

Outbreak of yellow fever in Angola

24 March 2016

Main conclusions and options for response

The advancing epidemic of yellow fever in Angola in the past five months highlights the risk of infection for unvaccinated travellers, and the risk of further international spread through introduction of the virus into areas with a competent vector and susceptible populations. The identification of yellow fever among returning travellers to China, Kenya, Mauritania and the Democratic Republic of Congo represents a significant risk of further international spread, even in areas where it has not been transmitted in the past, such as China.

Outbreaks of yellow fever in urban settings have the potential for rapid spread and constitute a public health emergency, requiring mass immunisation campaigns for containment purposes. In the long term, introducing preventive immunisation through routine childhood vaccination in endemic countries can significantly reduce the burden of the disease.

Advice to travellers

Vaccination against yellow fever is recommended for all those ≥ 9 months old travelling to areas where there is evidence of persistent or periodic yellow fever virus transmission. WHO publishes a list of countries, territories and areas with yellow fever vaccination requirements and recommendations. The yellow fever vaccine is recommended for travellers going to Angola. The country requirement specifies that a yellow fever vaccination certificate is required for travellers aged over 9 months. The certificate of yellow fever vaccination, which presently is valid for 10 years, will become valid for life in July 2016.

Prevention of importation

In the EU, the risk of yellow fever virus being introduced is limited to unvaccinated viraemic travellers coming from epidemic areas. Following the introduction of the virus, establishment of local transmission is possible in areas where *Aedes aegypti* mosquito is present and active. It is also possible in areas where *Aedes albopictus* is abundant, even though evidence supporting the *Aedes albopictus* mosquito's competence to transmit yellow fever is weaker.

Countries with receptive areas for yellow fever transmission (presence of the relevant, active mosquitoes and naïve population for yellow fever) should consider stipulating the requirement of a yellow fever vaccination certificate for travellers coming from affected areas during the mosquito season.

Studies assessing the competence of the European *Aedes albopictus* mosquito populations and the capacity to transmit yellow fever need to be reviewed.

Erratum, 30 March 2016
Reference numbering was corrected.

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Advice to clinicians

Clinicians should consider yellow fever among travellers returning from affected areas. Suspected and confirmed patients should be prevented from being bitten by *Aedes* mosquito vectors in areas where they are present (for example through the use of a mosquito net).

Laboratory capacity in the EU

There is sufficient capacity in the EU for the detection of yellow fever through several reference laboratories.

Prevention of spread in the EU

Countries with receptive areas for yellow fever transmission (presence of the active suitable mosquitoes and naïve population for yellow fever) should consider requiring yellow fever vaccination certificate for travellers coming from affected areas during the mosquito season.

Studies assessing the competence of the European *Aedes albopictus* mosquito populations and the capacity to transmit yellow fever need to be reviewed.

Source and date of request

ECDC Internal Decision, 21 March 2012.

Public health issue

This document assesses the risk of yellow fever infections in Europe related to the ongoing outbreak of yellow fever in Angola, and the notification of imported cases in China and possibly Mauritania.

Consulted experts

ECDC experts (in alphabetical order): Denis Coulombier, Niklas Danielsson, Alastair Donachie, Laura Espinosa, Laurence Marrama, Edit Szegedi, Hervé Zeller.

External expert: Gilles Pomerol (Global Capacities Alert and Response, WHO Geneva)

Disease background information

Yellow fever is an acute viral haemorrhagic vector-borne disease affecting humans and non-human primates in tropical areas of Africa and South America. It is caused by a virus of the Flavivirus genus of the Flaviviridae family and transmitted by infected mosquitoes of *Aedes* and *Haemagogus* genera.

The virus originates in Africa and was introduced to the Americas several hundred years ago. The disease is transmitted by several *Aedes* mosquito species in sylvatic cycles and by *Aedes aegypti* in urban cycles. Monkeys and humans act as amplifying hosts [1].

Yellow fever is endemic in 34 countries across sub-Saharan Africa and in 13 countries across South America, from Panama to the northern part of Argentina [2]. In 2013, there were an estimated 130 000 (95% CI 51 000–380 000) severe cases and 78 000 (95% CI 19 000–180 000) deaths in Africa [3], accounting for about 90% of the global cases [3]. Autochthonous transmission of yellow fever has never been detected in Asia.

In endemic countries, yellow fever is maintained in a cycle involving mosquitoes and non-human primates. Infected mosquitoes that bite humans entering the forest give rise to sporadic cases of yellow fever. Infected humans who return to urban areas where the highly effective and anthropophilic *Aedes aegypti* vector is present, may initiate human-to-human transmission cycles. Large epidemics, with tens of thousands of deaths, have been recorded in Africa.

Most infections in humans are either asymptomatic or result in mild illness. After an incubation period of typically three to six days, infection occurs in one or two phases. The initial symptoms include sudden onset of fever, chills, severe headache, back pain, general body aches, nausea, vomiting, fatigue and weakness. Most people improve after the first phase but after a brief remission around 15% of cases develop the severe form of the disease, characterised by high fever, jaundice, bleeding and eventually shock and multiple organ failure. Among those who develop severe disease, up to 50% may die. There is no specific treatment for yellow fever. Infection provides life-long immunity.

Yellow fever is difficult to diagnose, especially during the early stages, and differential diagnoses include: malaria, dengue, leptospirosis, viral hepatitis and poisoning. The virus can be detected in blood specimens by RT-PCR, antigen-capture or viral isolation. A serological diagnosis can be made by detection of specific IgM antibodies one week after infection [4].

Prevention and outbreak control

Yellow fever is effectively prevented through vaccination with the live attenuated vaccine that was first developed in 1937. A single dose is considered to provide lifelong protection [5]. The vaccine is recommended for people aged ≥ 9 months. Some adverse effects associated with the vaccine have been reported and a case-by-case assessment of the risks and benefits of yellow fever vaccination should be considered for some risk groups, such as older people or those with underlying health conditions [6].

The vaccine is recommended for individual protection of travellers at risk of exposure to yellow fever and to prevent international spread of the disease from endemic countries to countries with competent vectors.

The period of protection provided by yellow fever vaccination, and the term of validity of the certificate will soon change from 10 years to life for those vaccinated. This change will legally enter into force in July 2016 [7]. Until then, the International Health Regulation (IHR) 2005 will continue to specify that the validity period of yellow fever vaccination certificates is ten years from the date when the vaccination becomes effective (IHR 2005 Annex 7) [8].

A mass vaccination campaign is the most effective public health strategy to control yellow fever outbreaks. The yellow fever vaccine stockpile is managed by the International Coordinating Group on Vaccine Provision for Yellow Fever Control (Annex 1). Complementary preventive measures include using insect repellent and wearing protective clothing. Mosquito control can also help to prevent yellow fever, and is vital in situations where vaccination coverage is low or the vaccine is not immediately available. Mosquito control includes eliminating sites where mosquitoes can breed, and killing adult mosquitoes and larvae by using insecticides and larvicides in areas with high mosquito density. Community involvement through activities, such as cleaning household drains and covering water containers where mosquitoes can breed, is a very important and effective way to control mosquitoes [1].

Event background information

The first cases in the ongoing outbreak of yellow fever in Angola were reported on 5 December 2015 in the Viana municipality, Luanda province [9]. Yellow fever infection was initially confirmed in three patients by PCR at the Zoonosis and Emerging Disease Laboratory of the National Institute for Communicable Diseases in Johannesburg, South Africa and at the Pasteur Institute in Dakar, Senegal.

Since the initial cases were detected in Luanda province, there has been a rapid increase in the number of suspected cases recorded since mid-January 2016. Local transmission is no longer restricted to Luanda. As of 21 March 2016, 16 of 18 provinces across the country have reported suspected cases. According to WHO, 17 laboratory-confirmed cases have been detected in 10 districts of six provinces outside Luanda.

To date, at least 1 132 suspected and confirmed cases have been reported nationally, including 168 deaths. Of these cases, 375 are laboratory-confirmed. Transmission continues in Luanda and it remains the most affected province with 818 cases (281 confirmed), including 129 deaths. The number of cases from provinces other than Luanda is reported to be increasing [10].

The international spread of yellow fever cases from Angola has already been documented with imported cases identified among returning travellers in China, Kenya and the Democratic Republic of Congo (DRC). As of 22 March 2016, China has reported five imported cases, four in Beijing [11,12] and one in Shanghai [13]. According to media, one fatal imported case of yellow fever has been reported in Mauritania [14].

According to Chinese media, the Chinese Embassy in Angola issued an alert regarding the need for vaccination against yellow fever and stated that at least six Chinese citizens had died of yellow fever in Angola in 2016 [15].

Two previous outbreaks of yellow fever have been documented in Angola: one in 1971 (65 cases) and one in 1988 (37 cases).

An ongoing mass vaccination campaign that started on 2 February 2016 in Luanda province aims to vaccinate 6.7 million people. According to the most recent WHO situation report, administrative data indicate a vaccination coverage of 80% for the province of Luanda as of 14 March 2016. Further mass vaccination campaigns will be necessary because of spread to other areas of the country.

Angola requires proof of yellow fever vaccination for all arriving visitors aged one year and above. Fake yellow fever vaccination certificates are reported to have been issued and WHO issued an alert in February 2016 regarding the circulation of a fake yellow fever vaccine in South-East Asia.

There is currently no requirement for travellers returning to the EU from a yellow fever outbreak area to demonstrate proof of vaccination against yellow fever.

ECDC threat assessment for the EU

Risk for travellers to affected areas

The increasing number of reports of yellow fever cases among unvaccinated Chinese citizens who have returned to China from Angola is an indication of the risk of infection in the country and the risk of viraemic travellers importing the disease to areas with competent vectors. Any unvaccinated traveller or resident in an epidemic area is at risk of being infected. Currently, all regions in Angola should be considered as areas at high risk of transmission of yellow fever.

Risk of international spread

The evolution of the situation in Angola is of concern. The number of suspected cases may be underestimated as surveillance is reportedly not optimal, especially in areas along the border with adjacent countries.

Viraemic patients travelling to areas where suitable vectors and susceptible human populations are present pose a risk for establishment of local transmission. Such areas exist in most of the inter-tropical zones of Africa, the Americas and Asia. Yellow fever cases have been reported recently in travellers from Angola to China, Kenya, Mauritania and the Democratic Republic of Congo. Therefore, the risk of international spread within Africa and beyond is currently significant.

As yellow fever and dengue fever share the same mosquito vector, *Aedes aegypti*, any area where dengue has been transmitted could be suitable for establishment of local transmission of yellow fever if the virus is introduced by a viraemic traveller. This could be the case in southern China, where dengue virus transmission occurs during the warmer mosquito vector season, leading to local outbreaks in these areas.

Risk of importation to the EU

The risk of importation of yellow fever in Europe is limited, as EU travellers coming from affected areas are likely to have been immunised. However, in the past a few imported cases of yellow fever have been reported in Europe among unvaccinated travellers returning from Ivory Coast (Germany, 1999), Gambia (Belgium, 2001) and Ghana (Spain, 2009) [16,17]. Other travellers coming from affected areas, including citizens of these countries, may not have been vaccinated against yellow fever, and therefore may arrive in the EU/EEA and become viraemic as they develop yellow fever, creating a risk of that local transmission of yellow fever may become established.

Risk of spread in the EU

The risk of establishment of yellow fever in the EU/EEA is mainly related to areas where *Aedes aegypti* is present. The mosquito is established in the Overseas Countries and Territories (OCT), and Outermost Regions (OMR) of the EU, located in the yellow fever belt (inter-tropical area), as well as in the Black Sea region of Europe (http://ecdc.europa.eu/en/healthtopics/vectors/vector-maps/Pages/VBORNET_maps.aspx). There are uncertainties about the capacity of *Aedes albopictus* to transmit yellow fever. The competence of *Aedes albopictus* for the transmission of the yellow fever virus has been demonstrated in Brazil using a Brazilian strain of yellow fever virus. Brazilian *Aedes albopictus* mosquitoes were infected at rates similar to those of Brazilian *Aedes aegypti* and dissemination was observed in the salivary glands. Although these dissemination and infection rates are lower than those observed for *Aedes aegypti*, the ability of *Aedes albopictus* to transmit the yellow fever virus cannot be ruled out in areas where infestation and biting indexes are high [18-20]. The competence of European *Aedes albopictus* mosquito populations needs to be further assessed, but areas where *Aedes albopictus* is active in the EU/EEA should be considered as potential areas for local transmission of yellow fever, following the introduction of the virus through a viraemic traveller.

Conclusions and options for response

The advancing epidemic of yellow fever in Angola in the past five months highlights the risk of infection for unvaccinated travellers, and the risk of further international spread through introduction of the virus in areas with competent vector and susceptible populations. The identification of yellow fever among returning travellers to China, Kenya, Mauritania and the Democratic Republic of Congo represent a significant risk of further international spread, even in areas where it has not been transmitted in the past, such as China.

Outbreaks of yellow fever in urban settings have the potential for rapid spread and constitute a public health emergency requiring mass immunisation campaigns for containment purposes. In the long term, introducing preventive immunisation through routine childhood vaccination in endemic countries can significantly reduce the burden of the disease.

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The certificate of yellow fever vaccination which presently is valid for 10 years will become valid for life in July 2016.

Prevention of importation

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Countries with receptive areas for yellow fever transmission (presence of the relevant, active mosquitoes and naïve population for yellow fever) should consider stipulating the requirement of a yellow fever vaccination certificate for travellers coming from affected areas during the mosquito season.

Studies assessing the competence of the European *Aedes albopictus* mosquito populations and the capacity to transmit yellow fever need to be reviewed.

Advice to clinicians

Clinicians should consider yellow fever among travellers returning from affected areas. Suspected and confirmed patients should be prevented from being bitten by *Aedes* mosquito vectors in areas where they are present (for example through the use of a mosquito net).

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Annex 1

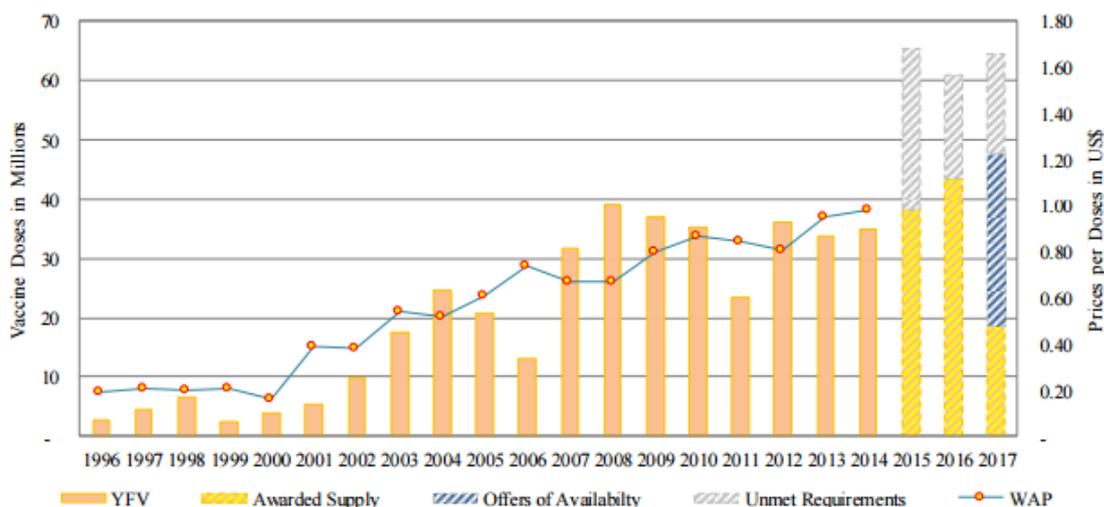
Yellow fever vaccine stockpile

The yellow fever stockpile is managed by the International Coordinating Group on Vaccine Provision for Yellow Fever Control (YF-ICG) with representatives from WHO, UNICEF, Médecins sans Frontières (MSF) and the International Federation of Red Cross and Red Crescent Societies (IFRC). The stockpile functions as a rotating stockpile for epidemic response [22]. Vaccines not used for epidemic response during a specified time period can be provided to at-risk countries for use in disease prevention campaigns [22].

Mosquito control includes eliminating sites where mosquitoes can breed, and killing adult mosquitoes and larvae by using insecticides in areas with high mosquito density. Community involvement through activities such as cleaning household drains and covering water containers where mosquitoes can breed is a very important and effective way to control mosquitoes [1].

Recently there has been concern regarding a possible shortage of yellow fever vaccine. According to UNICEF, the total country demand forecast for all vaccination activities worldwide for 2015–2017 was 64 million doses per year, but only 35 million are produced - 42% under the required quantity. Increased offers made to UNICEF for 2015–2017 will reduce some of this gap. UNICEF expects offered quantities to increase during subsequent years and it is anticipated that 47.6 million doses will be reached by 2017 (Figure 1) [23].

Figure 1. Yellow fever vaccine supply through UNICEF and demand forecast for 2015–2017



Source: UNICEF Supply Division/GA VI SDF v. 10

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