Towards the risk of yellow fever transmission in Europe

In light of the onset of the yellow fever (YF) outbreak in Brazil, the European Centre for Disease Prevention and Control (ECDC) estimated in January 2017 and March 2018 the risk of YF transmission in Europe as very low because of the low probability for the virus to be introduced by viraemic travellers to a European area with an established, competent, and active vector population [1].

However, the history of YF in Europe is proof that conditions have been suitable for transmission. Schaffner and Mathis [2] determined that in the 1950s Aedes aegypti, the species that best transmits the virus, was established in almost all Mediterranean countries, around the Black Sea and east of the Caspian Sea, which included both coastal and inland areas, as YF outbreaks were reported in harbour cities (Barcelona, Spain, and Saint-Nazaire in France in 1861, and Swansea in the UK in 1865) [2].

Although Ae. aegypti's current distribution still remains limited in Europe, it is expanding, possibly being a remnant of older Mediterranean populations [3] (Fig. 1A). This mosquito colonized Madeira in 2007, where it was responsible for a dengue epidemic in 2012 [4]; it has reappeared in parts of southern Russia and Georgia, in The Netherlands via airport and lastly in the Canary Islands [5]. This year a dengue epidemic has occurred in Egypt because of Ae. aegypti that might have originated from Saudi Arabia, having crossed the Red Sea on ships, or from Sudan via ground traffic [6]. There are no climatic or environmental reasons to prevent Ae. aegypti, if introduced by travel or trade, from surviving across southern Europe and becoming a competent vector for YF virus where temperatures are suitable for transmission, that is above 16.5°C, given the extended extrinsic incubation period of the virus at lower temperatures [7]. It is highly conceivable that Ae. aegypti could become re-established and widespread in Europe, as has happened in recent years with Ae. albopictus, whose geographical range was very limited 10 years ago (Fig. 1B,C).

Ae. albopictus is now widely settled in Europe (Fig. 1C) and has been reported as able to experimentally transmit YF. A significant amount of the virus was recently detected in the saliva of French Ae. albopictus mosquitoes 14 days after in vitro exposure [8]. Moreover, as observed with the A226V-mutated chikungunya virus strain at the start of its emergence in the Indian Ocean, the RNA virus of YF probably also has the capacity to adapt to local vectors by genetic mutations.

The ongoing Brazilian epizootic YF outbreak has spread in local populations with low vaccination coverage. Sylvatic transmission to humans has notably occurred in tourist areas such as the Island of Ilha Grande (state of Rio). There are around 2.4 million travellers every year between Europe and Brazil, and since the start of 2018 YF infection has been reported in six of them returning to The Netherlands, France, Romania, Switzerland, the UK, and Germany [9]. The virus has expanded to areas where YF was not traditionally considered to be a risk (Rio de Janeiro, Minas Gerais, and São Paulo), and consequently the vaccination campaign was started only after spread into a naive population (Center for Disease control (CDC) data https://wwwn.cdc.gov/travel/notices/alert/yellow-fever-brazil). The YF vaccine has high and lasting immunogenic properties. It is acceptably safe considering the lethality of the virus. Romano et al. reported six deaths for 5.5 million doses delivered during a campaign in an unvaccinated population in Brazil in 2008–2009 [10]. That's why YF vaccination should be better implemented in all the territories at risk of YF transmission [11], and could be enlarged in non-holoendemic countries and to neighbouring places in order to confine the virus and limit its globalization when epidemics occur.

These current events raise the issue of complete prophylaxis relying above all on the YF vaccine in travellers departing from and to YF endemic areas. Information on YF circulation and procedures for checking proof of vaccination should be provided at airports. Currently, there is a need to systematically screen for fever upon return and to test for YF if symptomatic within 2 weeks for each unvaccinated person coming back from epidemic areas. Biological samples must be collected according to biosafety procedures, taking all necessary precautions to avoid percutaneous exposure. Mandatory isolation under bed nets of all suspected cases must be immediately set up in association with adequate vector control measures in zones of confirmed vector activity. However, the question remains whether the YF virus could be imported and disseminated from asymptomatic or mildly symptomatic viraemic unvaccinated travellers.

The implementation of vaccination around an imported case in Europe during the active mosquito season is also of concern. In France, the Public Health Council (HCSP) discussed in February 2017 the appropriateness of post-exposition vaccination. Because of both a lack of vaccine doses and a low risk of local transmission, the HCSP retained only a potential indication to vaccinate individuals 200 metres around a documented autochthonous case in limited suitable conditions for local transmission. Since then, at least two French travellers have come back infected. Even if there is no study on the cost-effectiveness of a ring vaccination in this situation, it should be considered at the early step of YF importation, especially in the most at-risk European areas given the establishment of vectors, the climate, and the flow of travellers [11]. Use of fractional dose vaccines could be a relevant dose-sparing option in this aim to prevent the onset of an outbreak in non-endemic but high-risk places [12].
For all of these reasons, the risk of YF transmission in Europe, notably in the southern part, in the not too distant future, appears to have been underestimated. A gradient of risk should be assessed and monitored. A wider information and communication strategy to maximise awareness of populations and clinicians in case of local YF is crucial for prevention and detection and should be carefully examined.

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References

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