Yellow fever in Travelers

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Abstract:
Purpose of review: This decade has seen a resurgence of yellow fever (YF) that has also affected travelers with a record number of international travelers infected by YF virus including the first documented importation of YF into Asia.
Recent findings: The recent resurgence of YF has been attributed largely to sub-optimal vaccination coverage along with waning population-level immunity. With increasing YF cases in travelers, travel medicine providers need to familiarize themselves with the diagnosis and clinical management of severe YF. reinforce the generally acceptable safety profile of YF vaccine, but highlight the importance of continued physician and traveler education regarding the risks and benefits of YF vaccination, particularly for older travelers. There is an urgent need to better define "significant and unavoidable risk" for better benefit-risk assessments.

Key words: viscerotropic adverse events, neurotropism, risk-benefit assessment, travel

Introduction

Yellow fever is an old-age scourge, and one of the arboviral diseases associated with the highest case fatalities[1]. This decade has seen a resurgence of yellow fever (YF) that has also affected travelers with a record number of international travelers infected by YF virus returning to Europe and the US[2]. End 2015 to mid 2016, Angola experienced its biggest yellow fever outbreak for decades that rapidly spread via mobility networks within the country and to neighboring nations[3]. Towards the end of 2016, YF outbreaks emerged in close proximity to the most populated areas of metropolitan São Paulo and Rio de Janeiro in Brazil, thus posing an all-time high risk for rapid global spread via air travel. Health care professionals from non-endemic countries are therefore increasingly likely to see travelers with yellow fever. Here we review the risk of yellow fever in travelers, clinical management, as well as provide an update on the efficacy and safety yellow fever vaccines.

Epidemiology

Yellow fever is an acute infectious disease caused by the yellow fever virus, a flavivirus transmitted in tropical or subtropical areas, mainly through the bite of infected Aedes spp mosquitoes. YF is currently reported or has been reported in 34 countries in tropical Africa and 13 countries in the Americas, with sub-Saharan Africa carrying about 90% of the overall burden. Official reports of yellow fever incidence grossly underestimate the true number of cases, first of all because surveillance is based on the case definition of "fever and jaundice", but jaundice is not frequent even in severe yellow fever cases[4]; second, in many countries no surveillance systems exist, and third, a large proportion of yellow fever infections can be asymptomatic or mildly symptomatic, and difficult to differentiate clinically from other febrile illnesses in countries with limited resources for laboratory confirmation.

The recent resurgence of YF has been attributed largely to sub-optimal vaccination coverage along with waning population-level immunity[5]. Overall, substantial increases in YF vaccine coverage have occurred since 1970, but notable gaps still exist in coverage within risk zones, with around 400 million people still requiring vaccination in areas with YF virus transmission to achieve the 80% population coverage threshold recommended by WHO. The resulting gaps in YF vaccination coverage affect between 43% and 52% of the population within yellow fever risk zones[5, 6]. Lack in harmonized YF maps and the changing epidemiology of YF led to a collaborative WHO and CDC initiative in 2008-2010 to develop criteria and systematically apply such criteria for the designation of risk and specific changes to the classification of areas with risk of transmission of YF virus[7]. Four levels of YF risk were outlined and geographical areas were classified into the following categories: endemic, transitional, low potential for exposure, and no risk.

Risk in travelers

More than 9 million people from non-endemic countries in Asia, Europe, and North America travel to countries where YF is endemic, and these numbers are likely to increase given the increasing travel volumes globally[8]. Unvaccinated travelers who visit areas in Africa during periods of epidemic activity have an estimated risk of 1 in 267 and risk of death of 1 in 1333, although the risks are considerably lower during inter-epidemic periods[9]. Risk of illness and death for individuals travelling to South America is thought to be about ten times lower than it is for those travelling to Africa, because the lower rate of transmission in the jungle cycle in the Americas[9].

In recent years, the number of travelers importing yellow fever virus to non-endemic countries is at a record high[10]. Eleven unvaccinated Chinese working in Angola were infected with YF virus and exported the virus to China; the first documented exportation of

yellow fever via travelers to Asia[11]. Between January 2018 and December 2018, 10 travel-related cases of yellow fever, including four deaths, were reported in unvaccinated international travelers returning from Brazil[2]. Since then, two further cases were reported through GeoSentinel (GeoSentinel Director Dr David Hamer, personal communication). GeoSentinel is a global network of travel medicine providers that see ill returned travelers[12], and it set up to assess destination specific risks[13], risks by purpose of travel[14-17], and by diseases[18-22] and time trends[23]. Yellow fever was not reported in a descriptive analysis of life-threatening tropical diseases among 82,825 ill western travelers reported to GeoSentinel from June of 1996 to August of 2011[24]. Travelers' risk of acquiring YF is difficult to predict due to seasonal and epidemic variations, short duration of travel, ecologic determinants of virus transmission, immunity profiles, and activities. Overall however, the incidence of YF in travelers is very low, lower than most other vaccine-preventable travel related diseases [24-26], also because many travelers are protected through YF vaccination.

Clinical manifestations and clinical management

Clinical symptoms usually appear 3–6 days after a bite from an infected mosquito. YF virus first replicates in the site of inoculation, after which it spreads to the lymph nodes. It then travels to the liver, spleen, bone marrow, kidneys and myocardium but rarely spreads to the brain, exhibiting viscerotropic affinity. Typically, the disease onset is abrupt, with fever, muscle pain, particularly backache, headache, shivering, loss of appetite, and nausea or vomiting. Congestion of the conjunctivae and face are common, as well as relative bradycardia in the presence of fever[27]. In approximately 15% of infected persons, the illness recurs in more severe form after a brief remission of 2–24 hours[27]. YF can be a treacherous disease as its initial clinical presentation may be quite benign and non-specific, but can then take a fulminant course within a matter of a few days[28]. Clinicians need to be highly suspicious of YF, as earlier diagnosis may result in better management of this life-threatening disease.

Treatment of uncomplicated yellow fever is based on supportive clinical management. In mild disease, paracetamol is used to treat the symptoms of fever, myalgia and back pain and the patient can be managed at home. Salicylates and non-steroidal antiinflammatory drugs should be avoided because of the risk of gastrointestinal bleeding and platelet suppression.

Risk factors for developing more severe yellow fever include older age, high AST levels[29] and high neutrophil counts and YF viral load[30]. In the experience of the intensive care of a tertiary hospital in Sao Paolo, Brazil, during the recent YF outbreak, the fatality rate was 67%[4]. Patients with diabetes mellitus had a higher case fatality rate (CFR) of 80%, although

the difference was not significant due to the small sample size[4]. Leading causes of death were severe gastrointestinal bleeding, epileptic status, severe metabolic acidosis, pancreatitis, and multi-organ failure[4]. The following management lessons for severe YF were learnt from the Brazilian experience: Anticonvulsant drugs in patients with any symptoms of hepatic encephalopathy or arterial ammonia levels>70 μmol/L should be commenced, and therapeutic doses of intravenous proton pump inhibitors should be administered to present gastrointestinal bleeding. Other new therapy recommendations include early institution of plasma exchange[4].

Diagnosis

YF is difficult to diagnose clinically, especially during the early stages of the febrile disease. The differential diagnosis is wide and includes dengue[31], malaria, leptospirosis, viral hepatitis, and other haemorrhagic fevers. Incubation time and epidemiological clues are needed to raise the suspicion and request for laboratory confirmation. During the first days of illness, the diagnosis can be made by reverse transcriptase polymerase chain reaction (RT-PCR). However, laboratory diagnosis of YF is generally accomplished by testing serum to detect virus-specific IgM and neutralizing antibodies. A positive serological test for YF IgM is not sufficient to confirm a case[27]. If a person suspected of having YF tests positive for YF IgM, serology for other common flaviviruses should be carried out. Neutralizing antibody levels should be confirmed by using the plaque reducation neutralization test (PRNT), a more specific test for YF[32]. A history of recent vaccination needs to be taken into account when interpreting the results of YF testing. On 31 July 2018, the Centers for Disease Control (CDC) and WHO launched a trial version of a new ELISA test which is simpler and faster to perform. The new kit, called ELISA YF MAC HD, developed by CDC, ensures a standardized platform for yellow fever IgM testing, shortens the turnaround time from 2 days to just 3.5 h, but does not overcome the cross-reactivity issues with other flaviviruses[33].

Yellow Fever Vaccine

All currently YF vaccines are live attenuated viral vaccines from the 17D lineage based on a wild-type YF virus isolated in Ghana in 1927, developed more than 80 years ago by empirical passage in tissue culture, principally chicken embryo. The attenuated vaccine virus exists in 2 sub-strains (17D-204 and 17DD) which share 99.9% sequence homology[27]. Both sub-strains are used in vaccines prepared by culturing the virus in embryonated eggs, which is the main reason why YF vaccines are not rapidly scalable during an outbreak. The vaccine contains sorbitol and/or gelatine as a stabilizer and is lyophilized, without a preservative. Lyophilized vaccine should be stored and kept at 2–8 °C and reconstituted immediately before use with the sterile diluent provided by the manufacturer. After reconstitution, most

YF vaccines should be kept on ice, protected from sunlight, and discarded after 1–6 hours. YF vaccines are given as a single dose (0.5 ml) either subcutaneously or intramuscularly.

Currently there are five manufacturers: Sanofi Pasteur (for the North American and European market), Institut Pasteur in Senegal, Tiantan in China, Bio-Manguinhos/Fiocruz in Brasil, and –chukaov Institue in Russia. Only four manufacturers are WHO pre-qualified: Bio-Manguinhos, Institut Pasteur, Chumaov Institute and Sanofi Pasteur (Europe).

About 80%–100% of vaccine recipients develop protective levels of neutralizing antibodies within 10 days and 99% do so within 30 days[27]. Interestingly, no formal human efficacy studies have been performed with YF vaccine, however, 80 years of experience with ore than 600 million doses given attest to an extremely high efficacy. The systematic review that was the bases for WHO`s grading table[34] showed that since the introduction of YF vaccination in the 1930s, and following the administration of >540 million doses of vaccine since then, only 12 suspected cases of YF disease post vaccination have been identified[35].

Serious adverse events to Yellow Fever Vaccination

YF vaccines have been available since the 1930s, and are generally considered safe and effective. Of 666 respondents in a travel medicine clinic in Germany, 370 (55.6%) reported AEs, of which 258 (38.7%) were systemic and 230 (34.5%) were local. No severe AEs associated with YF vaccination were reported. Elderly vaccinees (aged >/=60 years) reported fewer total AEs than those aged <60 years (42.9% vs 60.3%;P < 0.001)[36]. However, reports on serious adverse reactions with severe clinical outcomes and even deaths emerged in the endemic population and travelers since 2001[37-39]. Yellow fever vaccine-associated viscerotropic disease (YEL-AVD) is a rare and serious adverse event of the yellow fever (YF) vaccine that mimics wild-type YF[37, 38]. The pathomechanism is poorly understood, but is likely not due to the impaired magnitude of adaptive immunity but instead to anomalies in the innate immune system and a possible disruption of the CCR5-RANTES axis[40]. Age and thymus dysfunction appear to be the main risk factors for YEL-AVD. Age-related regression of the thymus is associated with a decline in naive T cell output. This is thought to contribute to the reduction in T cell diversity seen in older individuals and linked with increased susceptibility to infection[41]. Autosomal recessive, complete IFNAR1 deficiency was also shown to result in life-threatening complications of vaccination with live attenuated measles and YF viruses in previously healthy individuals[42]. Adverse events following YF vaccination reported to the U.S. Vaccine Adverse Event Reporting System (VAERS) from 2007 through 2013 including age- and sex-specific reporting rates of all SAE, anaphylaxis, YF vaccine-associated neurologic disease (YEL-AND) and YF vaccine-associated viscerotropic disease (YEL-AVD) highlighted the following[43]: There were 938 adverse events following YF vaccination; of these, 84 (9%) were classified as SAEs for a rate of 3.8

per 100 000 doses distributed. Reporting rates of SAEs increased with increasing age with a rate of 6.5 per 100 000 in persons aged 60-69 years and 10.3 for >/=70 years. The rate for anaphylaxis was 1.3 per 100 000 doses distributed and was highest in persons </=18 years (2.7 per 100 000). Reporting rates of YEL-AND and YEL-AVD were 0.8 and 0.3 per 100 000, respectively; both rates increased with increasing age. These findings underpin the importance of continued physician and traveler education regarding the risks and benefits of YF vaccination, particularly for older travelers. YEL-AVD only occurs after primary vaccination.

Neurotropic serious averse reactions (YEL-AND) have been better characterized since 2001 with the development of case definitions, but have been known from 1950s in children younger than 9 months of age, an observation which led to the age restriction. YEL-AND is considered a collective group of clinical syndromes, and can be due to direct viral invasion of the central nervous system resulting in encephalitis or meningitis, or be due to a peripheral autoimmune complex (resulting in Guillain Barre Syndrome, acute disseminated encephalomyelitis or myelitis), or it can be due to a combination of both direct viral and autoimmune response. Risk factors are young and older age, although –unlike YEL-AVD, a greater proportion of cases have been in younger adults and those without obvious risk factors, hence, YEL-AND is more difficult to predict.

Limited data on the use of YF vaccination during pregnancy are available, and are usually derived from reports where pregnant women were either inadvertently vaccinated or given the vaccine during outbreaks. Two studies found no increased risk of major malformations or fetal death[44, 45]. However, an earlier study suggested a higher rate of spontaneous abortions with a relative risk of 2.3 among 39 pregnant women who received the vaccine [46]. HlV-infected patients with a CD4+ count > 200 cells/mm^3 do not have increased risk of AEs from YFV[47]. Safety of live vaccines in immmunocompromised travelers other than HIV is of particular interest. In one Swiss study, of 197 immunocompromised travelers 92 had received the YF vaccine, but reassuringly the incidence of systemic and local reactions were the same as when administered in healthy controls[48]. Some argue that we are possibly erring on the side of caution and under-vaccinating travelers who would benefit from YF vaccination[49]. Egg allergy vaccination protocols seem to provide a safe way to immunize patients with egg allergy[47].

Co-administration with other travel vaccines

Compact and short pre-travel immunization schedules, which include several vaccinations in a single visit, are desirable for many travelers[50]. However, concomitant vaccination could potentially compromise immunogenicity and/or safety of the individual vaccines and, therefore, possible vaccine interferences should be carefully assessed. Interference is

particularly of concern for two live vaccines. Given the current measles resurgence[51, 52] that may necessitate offering measles vaccination to adult travelers and migrants[53-56] who may also require YF vaccine demands more guidance on whether such vaccines can be co-administered on the same day or whether 28 days interval should be observed. Geometric mean titres for yellow fever were approximately three times higher among those who received MMR vaccinations 30 days later compared to concurrent administration of MMR and YF in a study in Brazil, suggesting that MMR and yellow fever vaccines should not be given on the same day[57]. In a phase 4, randomised, non-inferiority trial in Gambia infants aged 9-10 months who were randomly assigned to receive the IPV, measles-rubella, and yellow fever vaccines, singularly or in combinationshowed that YF antibody titres were reduced by co-administration but the seroconversion rates achieved non-inferiority [58]. Concurrent co-administration with inactivated vaccines is less of a problem. A recent study provided evidence that MenACWY-CRM can be administered with typhoid Vi polysaccharide vaccine and live attenuated YF vaccine without compromising antibody responses stimulated by the individual vaccines(NCT01466387)[59].

Duration of Protection, and controversies about the need for booster doses

In April 2013, the Strategic Advisory Group of Experts (SAGE) on immunization stated that a single dose of yellow fever (YF) vaccine is sufficient in the general population to confer a lifelong protection against YF. As the period of validity of the International Certificate of Vaccination (ICV) was extended to a lifetime in June 2016, no booster dose are officially needed. The rationale for this recommendation was based.on a systematic review by Gotuzzo et al which identified 6 studies indicating that a high proportion of vaccine recipients (>90%) have detectable levels of serum neutralizing antibodies up to 20 years post YF vaccination[35]. In 2015, the Advisory Committee on Immunization Practices (ACIP) in the US voted that a single primary dose of yellow fever vaccine provides long-lasting protection and is adequate for most travelers. ACIP also approved recommendations for at-risk laboratory personnel and certain travelers to receive additional doses of yellow fever vaccine. However, Amanna and Slifka argued based on epidemiological data on vaccine failures (particularly evident at >10 years after vaccination) that current recommendations to no longer administer YFV-17D booster vaccination should be carefully re-evaluated[60]. Seroconversion rates in infants aged 9 months are clearly lower than in adults, and this fact would suggest a booster dose at least 10 years later for those who received YF vaccination at the age of 9 months[61]. Few studies have assessed the duration of humoral immunity following yellow fever (YF) vaccination in a non-endemic populations such as travelers. A recent CDC study on the persistence of neutralizing antibodies to YF among 234 US travelers showed that among the 155 individuals vaccinated who were vaccinated <10 years prior to

serum collection, 146 (94%) had a positive PRNT compared with 82% (54/66) of individuals vaccinated >/=10 years prior to serum collection (P = 0.01)[62]. Post-vaccination PRNT titers showed a time-dependent decrease. Individuals with immune-compromising conditions were less likely to have a positive PRNT (77%) compared with those who were not immune-compromised (92%; P = 0.04) [62]. This study triggered several editorials and letters to the editor in the Journal of Travel Medicine arguing for two life-time doses[63, 64] versus following the WHO recommendations for one life time dose in travelers[65]. A booster dose could be considered for certain travelers with risk factors, persons living with HIV or other immuncoompromising conditions who are planning travel to high-risk areas based on immune competence and time since vaccination.

A prospective study determined the potential impact of the SAGE recommendations on the vaccination activity of travel clinics. The authors showed that among 1,037 subjects seen in three travel clinics for a YF vaccination in 2013, about 32.3% went for a booster dose that is no longer useful according to the revised SAGE recommendations. A drop in vaccination activity has to be expected by travel clinics in the next years, and changes in daily exercise have to be anticipated, as YF vaccination is a large part of the regular work of many healthcare providers specialized in travel medicine[66].

Vaccine shortage and fractional YF vaccines

Vaccine shortages for YF vaccine supply that affect travelers recur on a frequent basis[67], the most recent in North America due to a change in manufacturing in the US. Sanofi Pasteur, the manufacturer of the only yellow fever vaccine (YF-VAX) licensed in the US, announced that their stock of YF-VAX is totally depleted as of July 24, 2017. YF-VAX for civilian use will be unavailable for ordering from Sanofi Pasteur until mid-2018, when their new manufacturing facility is expected to be completed. However, YF-VAX might be available at some clinics for several months, until remaining supplies at those sites are exhausted. In anticipation of this temporary total depletion, in 2016, Sanofi Pasteur submitted an expanded access investigational new drug application to the Food and Drug Administration to allow for importation and use of Stamaril, the YF vaccine manufactured by Sanofi Pasteur in France[68]. Vaccine shortages in Western countries have also led to increasing uptake of fractional YF vaccines in travelers[69] despite the fact that such use is currently only WHO-endorsed in endemic populations for outbreak use.

Fractional Yellow Fever vaccine

All YF vaccines are all highly potent, with average doses between 10,00 and 44,000 international units (IU) — far above the WHO's recommended minimum of 1000 IU[70]. In

principle, the quantity of vaccine virus in fractional doses of standard vaccine would therefore still exceed the WHO's minimum requirement[70]. Based on this observation, WHO endorsed the use of 1/5 of the standard YF dose for outbreak situations when stockpiles have been depleted, which happened during the YF outbreak in Angola and DRC, and now also in Brazil. However, the potency varies from manufacturer to manufacturer and from batch to batch, and in particular varies from time since vaccine formulation, and hence various questions need to be addressed with regards to the immunogenicity and safety at doses just below the 1000 IU. The extent and duration of protection of fractional doses in populations such as children, pregnant women, persons with HIV and other co-morbidities that may result in different vaccine responses are currently unknown. The first study on 1/5th dose in children two years of age was conducted in DRC after the emergency roll-out of fractional doses, and reassuringly showed high seroconversion rates one month following SC administration[71].The results of studies comparing seroconversion rates after fractional-dose versus full-dose YF vaccination for each WHO-prequalified vaccine product (ClinicalTrials.gov number, NCT02991495), including in special populations such as children and persons living with HIV, are now much awaited[72]. Until those questions have been addressed, fractional YF vaccination is not yet compliant with the International Health Regulations. Should fractional YF vaccination be indeed equivalent to the standard dose, then the lower dose could become an antigen-sparing strategy of much broader utility[72].

International Health Regulations and Yellow Fever

Yellow fever is the only disease for which the WHO International Health Regulations (IHR) mandate proof of vaccination for travelers from countries where yellow fever is endemic to countries vulnerable for yellow fever, defined as the presence of suitable vectors[73]. An International Certificate of vaccination and prophylaxis (also commonly called Yellow card) is valid for a lifetime. Unfortunately, the 11 cases of exportation of YF via unvaccinated Chinese workers from Angola to China in 2016 show that the IHR regulations can be circumvented[74]. In fact, modelling studies show that none of the approximately 250,000 Chinese workers in Angola at the time of the YF outbreak were vaccinated[75].

Media reports of counterfeit markets abound. Yet, there is surprisingly little academic literature documenting the extent of this problem. Checks at airports and land crossing points appear to be non-systematic. In a study in Tanzania, checks were also performed in travelers who did not enter Tanzania from a YF-endemic country. No seasonal or daytime pattern could be identified; the thoroughness of checks varied widely. In the case of travel without valid YFV, an exemption certificate was always accepted[76]. It is of utmost urgency that governments turn their attention to enforcing the IHR.

Yellow fever risk in Asia

For travelers not complying with the IHR regulations, importation of the virus by a viremic traveler could initiate an enzootic transmission cycle, leading to a long-term infection risk for the local population. Although solid data on the extent of IHR circumvention is not available, it is likely that the 11 cases of importation from Angola to China will not remain the only cases. Why outbreaks of yellow fever have not yet occurred in Asia is unknown. The 11 cases were imported in China`s winter, hence vectorial capacity of Aedes mosquitoes was low[77]. Aedes aegypti, the more efficient vector than Aedes albopictus, does not exist in most parts of Europe, and hence Europe and largely the United States are less at risk, but it is not a zero risk, as YF outbreaks did occur in the Western hemisphere in the past[78]. With changing climate conditions, such a risk may increase[79, 80], further compounded by the fact that recently outbreaks have occurred around urban centers[81]. Is Asia prepared for a yellow fever epidemic? Competent vectors exist, but some cross-protection through Asia`s highly prevalent dengue seroprevalence exists[82]. Provided the relative vector competence is above 0.7, one infected traveler can introduce urban YF in a dengue endemic area beyond the current risk areas, as long as *Aedes aegypti* is present[83]. More studies are needed to understand the vectorial capacity and vector competence of *Aedes aegypti* in Asia. Furthermore, a better risk assessment is urgently needed for YF establishment in Asia. Strengthening of laboratory-based surveillance capable of detecting imported yellow fever, capacity to rapidly import vaccines should YF get established, and training healthcare workers in clinical management of severe yellow fever need to be urgently implemented[11, 84].

Pre-Travel advice:

YF vaccine is currently recommended for travel to 42 countries where YF is currently reported, or was reported in the past and where vectors/reservoirs remain. Risk assessment for travelers is a challenge and an evidence based GRADE approach is needed[85], in particular for low incidence but high impact diseases such as YF. The risk of vaccine adverse reactions have to be balanced against the risk of acquiring a disease with a high case fatality rate. The most common adverse reactions are similar to other live attenuated vaccines and include localized reactions, fever, headache, asthenia, malaise and myalgia, that are very common and generally mild and occur within one week of vaccination. No evidence exists to suggest that the reporting rates of allergic reactions is higher compared to other egg-derived vaccines. Viscerotropic and neurotropic reactions are the unique serious risks that need to be carefully explained to all travelers. All cases have been in primary vaccinees, and should therefore not occur with booster doses. Viscerotropic disease has a rapid onset, with rapid clinical

deterioration within 7 days and a fatality in reported cases up to 50%, usually within 10 days. Risk factors include older age, autoimmune disease, thymectomy for thymoma, systemic lupus erythematosus and pernicious anemia[86]. No clear risk factors have been recognized for neurotropic reactions, except for very young age.

It is very important to include travelers in the decision making process. Most travelers agreed they needed to understand destination-specific YF risks (82%) and vaccine risks (88%), and wanted to be involved in YF vaccine decisions (87%)[87]. The majority of registered travel agencies in Peru did not provide sufficient and accurate information regarding risk and prevention of YF to travelers[88]. Providers need effective risk communication skills and the ability to elicit and respond to travelers' concerns to help them make informed, shared decisions. For YF vaccines, this is particularly challenging given the uncertainties of true risk at destination versus YF vaccine associated adverse events. The risk is often unpredictable and variable for an individual person, and cannot be quantified with any certainty in real time given that new emergence of outbreaks can often also not be predicted. For example, the recent YF outbreak in Brazil occurred in a metropolitan area that was not really predicted, and required ad-hoc change in recommendations[89]. It is also important that travel medicine providers are not falsely reassured by the absence of YF case reports in certain destinations, as the absence of cases could reflect good vaccine coverage rather than absence of YF virus transmission[90]. Travel medicine practitioners need to ensure that there is indeed an indication for YF vaccination, and weigh up the risk of adverse events versus individual risk of acquiring YF during travel, dependent on duration, outbreak intensity, and activities during travel. For persons older than 60, and clearly for all persons with a history of thymus disease, a medical certificate should be issued stating that such travelers are exempt from vaccination. Travel medicine practitioners need to advise on alternative risk management measures including personal protective measures to avoid mosquito bites although compliance rates are notoriously low[91-93].

Conclusions:

References:

1. Chen LH, Kozarsky PE, Visser LG. What's old is new again: the re-emergence of yellow fever in Brazil and vaccine shortages. Clin Infect Dis. 2018. doi: 10.1093/cid/ciy777. PubMed PMID: 30204852.
2. Hamer DH, Angelo K, Caumes E, van Genderen PJJ, Florescu SA, Popescu CP, et al. Fatal Yellow Fever in Travelers to Brazil, 2018. MMWR Morb Mortal

Wkly Rep. 2018;67(11):340-1. doi: 10.15585/mmwr.mm6711e1. PubMed PMID: 29565840; PubMed Central PMCID: PMCPMC5868208.
3. Brent SE, Watts A, Cetron M, German M, Kraemer MU, Bogoch, II, et al. International travel between global urban centres vulnerable to yellow fever transmission. Bull World Health Organ. 2018;96(5):343-54B. doi: 10.2471/BLT.17.205658. PubMed PMID: 29875519; PubMed Central PMCID: PMCPMC5985425.
4. Ho YL, Joelsons D, Leite GFC, Malbouisson LMS, Song ATW, Perondi B, et al. Severe yellow fever in Brazil: clinical characteristics and management. J Travel Med. 2019. doi: 10.1093/jtm/taz040. PubMed PMID: 31150098.
5. Shearer FM, Moyes CL, Pigott DM, Brady OJ, Marinho F, Deshpande A, et al. Global yellow fever vaccination coverage from 1970 to 2016: an adjusted retrospective analysis. Lancet Infect Dis. 2017;17(11):1209-17. doi: 10.1016/S1473-3099(17)30419-X. PubMed PMID: 28822780; PubMed Central PMCID: PMCPMC5666204.
6. Wilder-Smith A. Yellow fever vaccination: estimating coverage. Lancet Infect Dis. 2017;17(11):1109-11. doi: 10.1016/S1473-3099(17)30494-2. PubMed PMID: 28822782.
7. Jentes ES, Poumerol G, Gershman MD, Hill DR, Lemarchand J, Lewis RF, et al. The revised global yellow fever risk map and recommendations for vaccination, 2010: consensus of the Informal WHO Working Group on Geographic Risk for Yellow Fever. Lancet Infect Dis. 2011;11(8):622-32. doi: 10.1016/S1473-3099(11)70147-5. PubMed PMID: 21798462.
8. Glaesser D, Kester J, Paulose H, Alizadeh A, Valentin B. Global travel patterns: an overview. J Travel Med. 2017;24(4). doi: 10.1093/jtm/tax007. PubMed PMID: 28637267.
9. Monath TP, Cetron MS. Prevention of yellow fever in persons traveling to the tropics. Clin Infect Dis. 2002;34(10):1369-78. doi: 10.1086/340104. PubMed PMID: 11981733.
10. Gubler DJ. Pandemic yellow fever: a potential threat to global health via travelers. J Travel Med. 2018;25(1). doi: 10.1093/jtm/tay097. PubMed PMID: 30299494.
11. Wilder-Smith A, Lee V, Gubler DJ. Yellow fever: is Asia prepared for an epidemic? Lancet Infect Dis. 2019;19(3):241-2. doi: 10.1016/S1473-3099(19)30050-7. PubMed PMID: 30833057.
12. Wilder-Smith A, Boggild AK. Sentinel Surveillance in Travel Medicine: 20 Years of GeoSentinel Publications (1999-2018). J Travel Med. 2018;25(1). doi: 10.1093/jtm/tay139. PubMed PMID: 30508133.
13. Angelo KM, Haulman NJ, Terry AC, Leung DT, Chen LH, Barnett ED, et al. Illness among US resident student travellers after return to the USA: a GeoSentinel analysis, 2007-17. J Travel Med. 2018;25(1). doi: 10.1093/jtm/tay074. PubMed PMID: 30202952; PubMed Central PMCID: PMCPMC6503850.
14. Bunn W. Business travel-associated illness: a geosentinel analysis. J Travel Med. 2018;25(1). doi: 10.1093/jtm/tay030. PubMed PMID: 29851453.
15. Chen LH, Leder K, Barbre KA, Schlagenhauf P, Libman M, Keystone J, et al. Business travel-associated illness: a GeoSentinel analysis. J Travel Med. 2018;25(1). doi: 10.1093/jtm/tax097. PubMed PMID: 29462444; PubMed Central PMCID: PMCPMC5824651.

16. McCarthy AE, Weld LH, Barnett ED, So H, Coyle C, Greenaway C, et al. Spectrum of illness in international migrants seen at GeoSentinel clinics in 1997-2009, part 2: migrants resettled internationally and evaluated for specific health concerns. Clin Infect Dis. 2013;56(7):925-33. doi: 10.1093/cid/cis1016. PubMed PMID: 23223602.
17. Boggild AK, Geduld J, Libman M, Yansouni CP, McCarthy AE, Hajek J, et al. Spectrum of illness in migrants to Canada: sentinel surveillance through CanTravNet. J Travel Med. 2019;26(2). doi: 10.1093/jtm/tay117. PubMed PMID: 30395252.
18. Leder K, Black J, O'Brien D, Greenwood Z, Kain KC, Schwartz E, et al. Malaria in travelers: a review of the GeoSentinel surveillance network. Clin Infect Dis. 2004;39(8):1104-12. doi: 10.1086/424510. PubMed PMID: 15486832.
19. Lederman ER, Weld LH, Elyazar IR, von Sonnenburg F, Loutan L, Schwartz E, et al. Dermatologic conditions of the ill returned traveler: an analysis from the GeoSentinel Surveillance Network. Int J Infect Dis. 2008;12(6):593-602. doi: 10.1016/j.ijid.2007.12.008. PubMed PMID: 18343180.
20. Michal Stevens A, Esposito DH, Stoney RJ, Hamer DH, Flores-Figueroa J, Bottieau E, et al. Clostridium difficile infection in returning travellers. J Travel Med. 2017;24(3). doi: 10.1093/jtm/taw099. PubMed PMID: 28355613; PubMed Central PMCID: PMCPMC5697897.
21. Barbosa F, Barnett ED, Gautret P, Schlagenhauf P, van Genderen PJ, Grobusch MP, et al. Bordetella pertussis infections in travelers: data from the GeoSentinel global network. J Travel Med. 2017;24(3). doi: 10.1093/jtm/taw094. PubMed PMID: 28355615.
22. Salzer HJF, Stoney RJ, Angelo KM, Rolling T, Grobusch MP, Libman M, et al. Epidemiological aspects of travel-related systemic endemic mycoses: a GeoSentinel analysis, 1997-2017. J Travel Med. 2018;25(1). doi: 10.1093/jtm/tay055. PubMed PMID: 30085265; PubMed Central PMCID: PMCPMC6628256.
23. Leder K, Torresi J, Libman MD, Cramer JP, Castelli F, Schlagenhauf P, et al. GeoSentinel surveillance of illness in returned travelers, 2007-2011. Ann Intern Med. 2013;158(6):456-68. doi: 10.7326/0003-4819-158-6-201303190-00005. PubMed PMID: 23552375; PubMed Central PMCID: PMCPMC4629801.
24. Jensenius M, Han PV, Schlagenhauf P, Schwartz E, Parola P, Castelli F, et al. Acute and potentially life-threatening tropical diseases in western travelers--a GeoSentinel multicenter study, 1996-2011. Am J Trop Med Hyg. 2013;88(2):397-404. doi: 10.4269/ajtmh.12-0551. PubMed PMID: 23324216; PubMed Central PMCID: PMCPMC3583336.
25. Steffen R. Travel vaccine preventable diseases-updated logarithmic scale with monthly incidence rates. J Travel Med. 2018;25(1). doi: 10.1093/jtm/tay046. PubMed PMID: 30016468.
26. Angelo KM, Kozarsky PE, Ryan ET, Chen LH, Sotir MJ. What proportion of international travellers acquire a travel-related illness? A review of the literature. J Travel Med. 2017;24(5). doi: 10.1093/jtm/tax046. PubMed PMID: 28931136; PubMed Central PMCID: PMCPMC5825178.
27. WHO. Vaccines and vaccination against yellow fever-WHO position paper. Weekly Epidemiological Records. 2013;87(6):1112-5.

28. Kallas EG, Wilder-Smith A. Managing severe yellow fever in the intensive care: lessons learnt from Brazil. J Travel Med. 2019. doi: 10.1093/jtm/taz043. PubMed PMID: 31180486; PubMed Central PMCID: PMCPMC6621914.
29. Tuboi SH, Costa ZG, da Costa Vasconcelos PF, Hatch D. Clinical and epidemiological characteristics of yellow fever in Brazil: analysis of reported cases 1998-2002. Trans R Soc Trop Med Hyg. 2007;101(2):169-75. doi: 10.1016/j.trstmh.2006.04.001. PubMed PMID: 16814821.
30. Kallas EG, D'Elia Zanella L, Moreira CHV, Buccheri R, Diniz GBF, Castineiras ACP, et al. Predictors of mortality in patients with yellow fever: an observational cohort study. Lancet Infect Dis. 2019. doi: 10.1016/S1473-3099(19)30125-2. PubMed PMID: 31104909.
31. Wilder-Smith A, Ooi EE, Horstick O, Wills B. Dengue. Lancet. 2019;393(10169):350-63. doi: 10.1016/S0140-6736(18)32560-1. PubMed PMID: 30696575.
32. Goncalves A, Peeling RW, Chu MC, Gubler DJ, de Silva AM, Harris E, et al. Innovative and New Approaches to Laboratory Diagnosis of Zika and Dengue: A Meeting Report. J Infect Dis. 2018;217(7):1060-8. doi: 10.1093/infdis/jix678. PubMed PMID: 29294035; PubMed Central PMCID: PMCPMC6279137.
33. Leong WY. New diagnostic tools for yellow fever. J Travel Med. 2018;25(1). doi: 10.1093/jtm/tay079. PubMed PMID: 30184173.
34. . Available from: http://www.who.int/entity/immunization/position_papers/yellow_fever_duration_of_protection_immuno-competent.pdf.
35. Gotuzzo E, Yactayo S, Cordova 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;89(3):434-44. doi: 10.4269/ajtmh.13-0264. PubMed PMID: 24006295; PubMed Central PMCID: PMCPMC3771278.
36. Tanizaki R, Ujiie M, Hori N, Kanagawa S, Kutsuna S, Takeshita N, et al. Comparative study of adverse events after yellow fever vaccination between elderly and non-elderly travellers: questionnaire survey in Japan over a 1-year period. J Travel Med. 2016;23(3). doi: 10.1093/jtm/taw012. PubMed PMID: 27021495.
37. Leung WS, Chan MC, Chik SH, Tsang TY. First case of yellow fever vaccine-associated viscerotropic disease (YEL-AVD) in Hong Kong. J Travel Med. 2016;23(4). doi: 10.1093/jtm/taw020. PubMed PMID: 27087559.
38. van de Pol EM, Gisolf EH, Richter C. A case suspected for yellow fever vaccine-associated viscerotropic disease in the Netherlands. J Travel Med. 2014;21(6):421-4. doi: 10.1111/jtm.12135. PubMed PMID: 24920138.
39. Vasconcelos PF, Luna EJ, Galler R, Silva LJ, Coimbra TL, Barros VL, et al. Serious adverse events associated with yellow fever 17DD vaccine in Brazil: a report of two cases. Lancet. 2001;358(9276):91-7. PubMed PMID: 11463409.
40. Pulendran B, Miller J, Querec TD, Akondy R, Moseley N, Laur O, et al. Case of yellow fever vaccine--associated viscerotropic disease with prolonged viremia, robust adaptive immune responses, and polymorphisms in CCR5 and RANTES genes. J Infect Dis. 2008;198(4):500-7. doi: 10.1086/590187. PubMed PMID: 18598196; PubMed Central PMCID: PMCPMC3734802.
41. Palmer DB. The effect of age on thymic function. Front Immunol. 2013;4:316. doi: 10.3389/fimmu.2013.00316. PubMed PMID: 24109481; PubMed Central PMCID: PMCPMC3791471.

42. Hernandez N, Bucciol G, Moens L, Le Pen J, Shahrooei M, Goudouris E, et al. Inherited IFNAR1 deficiency in otherwise healthy patients with adverse reaction to measles and yellow fever live vaccines. J Exp Med. 2019. doi: 10.1084/jem.20182295. PubMed PMID: 31270247.
43. Lindsey NP, Rabe IB, Miller ER, Fischer M, Staples JE. Adverse event reports following yellow fever vaccination, 2007-13. J Travel Med. 2016;23(5). doi: 10.1093/jtm/taw045. PubMed PMID: 27378369.
44. Cavalcanti DP, Salomao MA, Lopez-Camelo J, Pessoto MA, Campinas Group of Yellow Fever Immunization during P. Early exposure to yellow fever vaccine during pregnancy. Trop Med Int Health. 2007;12(7):833-7. doi: 10.1111/j.1365-3156.2007.01851.x. PubMed PMID: 17596249.
45. Suzano CE, Amaral E, Sato HK, Papaiordanou PM, Campinas Group on Yellow Fever Immunization during P. The effects of yellow fever immunization (17DD) inadvertently used in early pregnancy during a mass campaign in Brazil. Vaccine. 2006;24(9):1421-6. doi: 10.1016/j.vaccine.2005.09.033. PubMed PMID: 16236402.
46. Nishioka Sde A, Nunes-Araujo FR, Pires WP, Silva FA, Costa HL. Yellow fever vaccination during pregnancy and spontaneous abortion: a case-control study. Trop Med Int Health. 1998;3(1):29-33. PubMed PMID: 9484965.
47. Porudominsky R, Gotuzzo EH. Yellow fever vaccine and risk of developing serious adverse events: a systematic review. Rev Panam Salud Publica. 2018;42:e75. doi: 10.26633/RPSP.2018.75. PubMed PMID: 31093103; PubMed Central PMCID: PMCPMC6386100.
48. Huber F, Ehrensperger B, Hatz C, Chappuis F, Buhler S, Eperon G. Safety of live vaccines on immunosuppressive or immunomodulatory therapy-a retrospective study in three Swiss Travel Clinics. J Travel Med. 2018;25(1). doi: 10.1093/jtm/tax082. PubMed PMID: 29394383.
49. de Jong W, de Man RA, Dalm V, Reusken C, Goeijenbier M, van Gorp ECM. Yellow fever vaccination for immunocompromised travellers: unjustified vaccination hesitancy? J Travel Med. 2019. doi: 10.1093/jtm/taz015. PubMed PMID: 30850844.
50. Yates JA, Rao SR, Walker AT, Esposito DH, Sotir M, LaRocque RC, et al. Characteristics and Preparation of the Last-Minute Traveler: Analysis of Vaccine Usage in the Global TravEpiNet Consortium. J Travel Med. 2019. doi: 10.1093/jtm/taz031. PubMed PMID: 31044254.
51. Leong WY. Measles cases hit record high in Europe in 2018. J Travel Med. 2018;25(1). doi: 10.1093/jtm/tay080. PubMed PMID: 30184169.
52. Massad E. Measles and human movement in Europe. J Travel Med. 2018;25(1). doi: 10.1093/jtm/tay091. PubMed PMID: 30312454.
53. Heywood AE. Measles: a re-emerging problem in migrants and travellers. J Travel Med. 2018;25(1). doi: 10.1093/jtm/tay118. PubMed PMID: 30395260.
54. Ceccarelli G, Vita S, Riva E, Cella E, Lopalco M, Antonelli F, et al. Susceptibility to measles in migrant population: implication for policy makers. J Travel Med. 2018;25(1). doi: 10.1093/jtm/tax080. PubMed PMID: 29232456.
55. Angelo KM, Libman M, Gautret P, Barnett E, Grobusch MP, Hagmann SHF, et al. The rise in travel-associated measles infections - GeoSentinel, 2015-2019. J Travel Med. 2019. doi: 10.1093/jtm/taz046. PubMed PMID: 31218359.
56. Staehelin C, Chernet A, Sydow V, Piso RJ, Suter-Riniker F, Funez S, et al. Seroprotection rates of vaccine-preventable diseases among newly arrived

Eritrean asylum seekers in Switzerland: a cross-sectional study. J Travel Med. 2019. doi: 10.1093/jtm/taz035. PubMed PMID: 31094415.
57. Nascimento Silva JR, Camacho LA, Siqueira MM, Freire Mde S, Castro YP, Maia Mde L, et al. Mutual interference on the immune response to yellow fever vaccine and a combined vaccine against measles, mumps and rubella. Vaccine. 2011;29(37):6327-34. doi: 10.1016/j.vaccine.2011.05.019. PubMed PMID: 21640779.
58. Clarke E, Saidu Y, Adetifa JU, Adigweme I, Hydara MB, Bashorun AO, et al. Safety and immunogenicity of inactivated poliovirus vaccine when given with measles-rubella combined vaccine and yellow fever vaccine and when given via different administration routes: a phase 4, randomised, non-inferiority trial in The Gambia. Lancet Glob Health. 2016;4(8):e534-47. doi: 10.1016/S2214-109X(16)30075-4. PubMed PMID: 27364568.
59. Alberer M, Burchard G, Jelinek T, Reisinger E, Beran J, Hlavata LC, et al. Safety and immunogenicity of typhoid fever and yellow fever vaccines when administered concomitantly with quadrivalent meningococcal ACWY glycoconjugate vaccine in healthy adults. J Travel Med. 2015;22(1):48-56. doi: 10.1111/jtm.12164. PubMed PMID: 25308927.
60. Amanna IJ, Slifka MK. Questions regarding the safety and duration of immunity following live yellow fever vaccination. Expert Rev Vaccines. 2016;15(12):1519-33. doi: 10.1080/14760584.2016.1198259. PubMed PMID: 27267203; PubMed Central PMCID: PMCPMC5171234.
61. Idoko OT, Mohammed N, Ansah P, Hodgson A, Tapia MD, Sow SO, et al. Antibody responses to yellow fever vaccine in 9 to 11-month-old Malian and Ghanaian children. Expert Rev Vaccines. 2019:1-9. doi: 10.1080/14760584.2019.1640118. PubMed PMID: 31269829.
62. Lindsey NP, Horiuchi KA, Fulton C, Panella AJ, Kosoy OI, Velez JO, et al. Persistence of yellow fever virus-specific neutralizing antibodies after vaccination among US travellers. J Travel Med. 2018;25(1). doi: 10.1093/jtm/tay108. PubMed PMID: 30346562.
63. Plotkin SA. Ten yearly yellow fever booster vaccinations may still be justified. J Travel Med. 2018;25(1). doi: 10.1093/jtm/tay130. PubMed PMID: 30462249.
64. Neumayr A, Staehelin C, Kuenzli E, Hatz C. Arguments for a two-dose yellow fever vaccination regimen in travellers. J Travel Med. 2019. doi: 10.1093/jtm/taz004. PubMed PMID: 30657977.
65. Visser LG, Veit O, Chen LH. Waning immunity after single dose yellow fever vaccination. Who needs a second shot? J Travel Med. 2018. doi: 10.1093/jtm/tay134. PubMed PMID: 30476151.
66. Wyplosz B, Leroy JP, Derradji O, Consigny PH. No booster dose for yellow fever vaccination: what are the consequences for the activity of vaccination in travel clinics? J Travel Med. 2015;22(2):140-1. doi: 10.1111/jtm.12173. PubMed PMID: 25384441.
67. Chen LH, Hamer DH. Vaccination Strategies During Shortages of Yellow Fever Vaccine-Reply. JAMA. 2018;319(12):1280-1. doi: 10.1001/jama.2018.0232. PubMed PMID: 29584837.
68. Gershman MD, Sotir MJ. Update: Temporary Total Depletion of U.S. Licensed Yellow Fever Vaccine for Civilian Travelers Addressed by Investigational New Drug Use of Imported Stamaril Vaccine. MMWR Morb Mortal

Wkly Rep. 2017;66(29):780. doi: 10.15585/mmwr.mm6629a4. PubMed PMID: 28749924; PubMed Central PMCID: PMCPMC5657809.
69. Teitelbaum P, Bui YG, Libman M, McCarthy A. Fractional dosing of yellow fever vaccine during shortages: perspective from Canada. J Travel Med. 2018;25(1). doi: 10.1093/jtm/tay098. PubMed PMID: 30346564.
70. Vannice K, Wilder-Smith A, Hombach J. Fractional-Dose Yellow Fever Vaccination - Advancing the Evidence Base. N Engl J Med. 2018;379(7):603-5. doi: 10.1056/NEJMp1803433. PubMed PMID: 29995585.
71. Ahuka-Mundeke S, Casey RM, Harris JB, Dixon MG, Nsele PM, Kizito GM, et al. Immunogenicity of Fractional-Dose Vaccine during a Yellow Fever Outbreak - Preliminary Report. N Engl J Med. 2018. doi: 10.1056/NEJMoa1710430. PubMed PMID: 29443626.
72. Wilder-Smith A, Barrett A, Vannice K, Hombach J. Long-Term Protection After Fractional-Dose Yellow Fever Vaccination. Ann Intern Med. 2019;171(2):145-6. doi: 10.7326/L19-0196. PubMed PMID: 31307078.
73. Wilder-Smith A, Hill DR, Freedman DO. The revised International Health Regulations (2005): impact on yellow fever vaccination in clinical practice. Am J Trop Med Hyg. 2008;78(3):359-60. PubMed PMID: 18337324.
74. Wilder-Smith A, Leong WY. Importation of yellow fever into China: assessing travel patterns. J Travel Med. 2017;24(4). doi: 10.1093/jtm/tax008. PubMed PMID: 28426111.
75. Wilder-Smith A, Massad E. Estimating the number of unvaccinated Chinese workers against yellow fever in Angola. BMC Infect Dis. 2018;18(1):185. doi: 10.1186/s12879-018-3084-y. PubMed PMID: 29665797; PubMed Central PMCID: PMCPMC5905133.
76. Schonenberger S, Hatz C, Buhler S. Unpredictable checks of yellow fever vaccination certificates upon arrival in Tanzania. J Travel Med. 2016;23(5). doi: 10.1093/jtm/taw035. PubMed PMID: 27296582.
77. Liu-Helmersson J, Stenlund H, Wilder-Smith A, Rocklov J. Vectorial capacity of Aedes aegypti: effects of temperature and implications for global dengue epidemic potential. PLoS One. 2014;9(3):e89783. doi: 10.1371/journal.pone.0089783. PubMed PMID: 24603439; PubMed Central PMCID: PMCPMC3946027.
78. Reiter P. Yellow fever and dengue: a threat to Europe? Euro Surveill. 2010;15(10):19509. PubMed PMID: 20403310.
79. Lillepold K, Rocklov J, Liu-Helmersson J, Sewe M, Semenza JC. More arboviral disease outbreaks in continental Europe due to the warming climate? J Travel Med. 2019. doi: 10.1093/jtm/taz017. PubMed PMID: 30850834.
80. Semenza JC, Ebi KL. Climate change impact on migration, travel, travel destinations and the tourism industry. J Travel Med. 2019. doi: 10.1093/jtm/taz026. PubMed PMID: 30976790.
81. Wilder-Smith A, Monath TP. Responding to the threat of urban yellow fever outbreaks. Lancet Infect Dis. 2017;17(3):248-50. doi: 10.1016/S1473-3099(16)30588-6. PubMed PMID: 28017560.
82. Izurieta RO, Macaluso M, Watts DM, Tesh RB, Guerra B, Cruz LM, et al. Anamnestic immune response to dengue and decreased severity of yellow Fever. J Glob Infect Dis. 2009;1(2):111-6. doi: 10.4103/0974-777X.56257. PubMed PMID: 20300401; PubMed Central PMCID: PMCPMC2840959.

83. Ribeiro AF, Tengan C, Sato HK, Spinola R, Mascheretti M, Franca AC, et al. A public health risk assessment for yellow fever vaccination: a model exemplified by an outbreak in the state of Sao Paulo, Brazil. Mem Inst Oswaldo Cruz. 2015;110(2):230-4. doi: 10.1590/0074-02760140345. PubMed PMID: 25946247; PubMed Central PMCID: PMCPMC4489454.
84. Wilder-Smith A, Chen LH, Melo A, Visser LG. Improving clinical management of patients with severe yellow fever. Lancet Infect Dis. 2019;19(7):678-9. doi: 10.1016/S1473-3099(19)30122-7. PubMed PMID: 31104910.
85. Torresi J, Steffen R. Redefining priorities towards graded travel-related infectious disease research. J Travel Med. 2017;24(6). doi: 10.1093/jtm/tax064. PubMed PMID: 29088486.
86. Seligman SJ. Risk groups for yellow fever vaccine-associated viscerotropic disease (YEL-AVD). Vaccine. 2014;32(44):5769-75. doi: 10.1016/j.vaccine.2014.08.051. PubMed PMID: 25192973.
87. Lown BA, Chen LH, Han PV, Jentes ES, Wilson ME, Benoit CM, et al. Preferences and decision needs of Boston-area travelers to countries with risk of Yellow fever virus transmission: implications for health care providers. J Travel Med. 2014;21(4):266-71. doi: 10.1111/jtm.12119. PubMed PMID: 24734961.
88. Villanueva-Meyer PG, Garcia-Jasso CA, Springer CA, Lane JK, Su BS, Hidalgo IS, et al. Advice on malaria and yellow fever prevention provided at travel agencies in Cuzco, Peru. J Travel Med. 2015;22(1):26-30. doi: 10.1111/jtm.12149. PubMed PMID: 25156197.
89. Fujita DM, da Silva Nali LH, Salvador FS, de Andrade Junior HF. Recommendations for travellers during the yellow fever outbreaks in Brazil-2018. J Travel Med. 2018;25(1). doi: 10.1093/jtm/tay016. PubMed PMID: 29635644.
90. Monath TP, Gershman M, Hill DR, Marano N, Staples JE, Wilder-Smith A. Yellow fever recommendations for tourists to Kenya: a flawed risk assessment. J Travel Med. 2009;16(2):146; author reply -7. doi: 10.1111/j.1708-8305.2008.00295_1.x. PubMed PMID: 19335822.
91. Lalani T, Yun H, Tribble D, Ganesan A, Kunz A, Fairchok M, et al. A comparison of compliance rates with anti-vectorial protective measures during travel to regions with dengue or chikungunya activity, and regions endemic for Plasmodium falciparum malaria. J Travel Med. 2016;23(5). doi: 10.1093/jtm/taw043. PubMed PMID: 27378367; PubMed Central PMCID: PMCPMC4939934.
92. Goodyer L, Schofield S. Mosquito repellents for the traveller: does picaridin provide longer protection than DEET? J Travel Med. 2018;25(suppl_1):S10-S5. doi: 10.1093/jtm/tay005. PubMed PMID: 29718433.
93. Goodyer L, Song J. Mosquito bite-avoidance attitudes and behaviors in travelers at risk of malaria. J Travel Med. 2014;21(1):33-8. doi: 10.1111/jtm.12053. PubMed PMID: 24383652.