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To vaccinate or let it be – current recommendations and the reality about yellow fever vaccination

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Recommendations to travellers regarding yellow fever vaccination (YFV) are based on personal risk, previous vaccinations, health status of the traveller and border regulations. Recently, WHO extended the recommendation regarding protection after YFV from 10 years to lifelong. We present the results of a survey among Swiss tropical and travel medicine experts, in which they were asked to decide upon the correct vaccination approach in eight case scenarios.

YFV is one of the most often administered vaccines in travel medicine [1] (40,000 doses per year in Switzerland [personal communication]). With over 600 million administered doses worldwide, only 12 yellow fever (YF) cases have been described in vaccinated persons [2]. Generally, YFV is well tolerated, but severe reactions, such as yellow fever vaccination-associated viscerotropic disease (YEL-AVD) or yellow fever vaccination-associated neurotropic disease (YEL-AND) occur in around 0.5/100,000 distributed doses [3]. In order to assess and harmonise indications for yellow fever vaccination, a survey was performed during a meeting of The Swiss Society of Tropical and Travel Medicine in January 2014. Experts assessed eight real and imaginary cases of travellers on whether YFV should be given, not given, or if a written exemption should be issued. Only one answer was possible and delay or cancellation of the trip was not an option.

Physicians were asked to give a recommendation for two scenarios: (i.) sufficient vaccine doses available and (ii.) shortage of YFV, as this was a problem at that time.

Overall, 55 questionnaires were distributed, and 43 (78%) were returned. Case descriptions, survey results and the correct options according to Swiss vaccination recommendations (version October 2013 [4]) are summarised in table 1.

Cases in detail

1. + 2. There is no risk of YF infection for wife and husband. For the wife's transit, no vaccination or exemption is necessary. The husband needs YFV or an exemption certificate, depending on the availability of YFV.

Independent of YFV availability, 60% of the specialists decided not to immunise the wife. More than 35% favoured an exemption in case of vaccine shortage or would have vaccinated. In case of vaccination, the wife would have been exposed to an unnecessary risk, especially, as persons aged 60 years and above have an increased risk of YEL-AVD [5]. For the husband, almost 90% opted for vaccination in scenario (i.) and around 70% for an exemption in scenario (ii.), i.e., a majority chose the correct answer according to current recommendations.

3. During pregnancy, YFV is generally not recommended although teratogenic effects have not been described [6]. The decision on vaccination during pregnancy has to be taken after an individual risk/benefit assessment [7]. As São Paulo and Rio de Janeiro are YF free and Iguaçu has a very low YF endemicity [8], the correct approach according to Swiss recommendations would be to abstain from YFV, in both vaccine availability scenarios. As YFV is not mandatory for a trip to Brazil, an exemption certificate is unnecessary.

Around 60% of respondents decided not to immunise in both scenarios; still more than a third opted for an unneeded exemption. Although not harmful, it brings along additional costs for the traveller as well as unnecessary workload.

4. As Cameroon has a moderate YF endemicity [8], Swiss recommendations would rather favour YFV in this pregnant woman regardless of vaccine availability depending on her destination within Cameroon. However, this decision might be arguable.

Around 40% of specialists decided to vaccinate in both scenarios. A larger group opted for an exemption. Still, in case of sufficient vaccine supplies, 5% chose not to vaccinate without handing out an

exemption. This decision may cause problems, as YFV is mandatory for entering Cameroon.

5. The traveller is not exposed to YF during this trip, but Thailand requires YFV when entry occurs within 10 days after visiting an endemic country. In the case of sufficient vaccine supplies, YFV is recommended; otherwise an exemption should be issued.
   More than 90% correctly decided to vaccinate the traveller in scenario (i); in scenario (ii), half of the respondents correctly opted for an exemption. In both scenarios, some specialists decided neither to vaccinate nor to exempt, leaving the traveller at risk of not being able to enter Thailand.
6. YFV is contraindicated under azathioprine/6–mercaptopurine [9]. Also, issuing an exemption is not recommended owing to the high YF infection risk; hence, this trip should not be undertaken. In both scenarios, around 70% would have issued an exemption. However, it is alarming that more than 20% decided to vaccinate endangering the immunosuppressed traveller due to the replication capacity of the attenuated vaccine strain. A minority would have not vaccinated without issuing an exemption.
7. According to 2013 WHO recommendations, a single YFV dose provides lifelong protection [7], even if a person started immunosuppressive medication afterwards. Therefore, an exemption should be issued to enter Ethiopia, as YFV is mandatory coming from an YF endemic country.
   A majority chose the correct answer; however, more than a quarter decided not to issue an exemption despite Ethiopian regulations. In scenario (i), 10% of experts would have given YFV even though it is clearly contraindicated under immunosuppression [9].
8. This traveller is still protected from the vaccine dose he received in 1973 according to WHO recommendations [7]. According to entry regulations, neither vaccination nor exemption is necessary if entering Kenya directly from Europe.
   Around 20% responded to vaccinate the traveller in scenario (i), although unnecessary by new WHO recommendations [7].

In our survey, delay or cancellation of a trip or interrupting immunosuppressive medication was not an option; however, in real life this will sometimes (but not always!) be a solution, as was also indicated by several comments on the questionnaires.

Overall, we saw that even among experts in a country with one of the highest travel frequencies, great uncertainty exists regarding the indication for YFV. Partly, these disagreements or uncertainties are provoked by the new WHO recommendations as well as conflicting border regulations. The Strategic Advisory Group of Experts on Immunization of the WHO stated in May 2013 that a single YFV dose confers lifelong protection (opposed to the previous 10-year recommendation). This decision is still viewed with scepticism among experts [10, 11] as studies looking at long-term immunity after YFV show conflicting results (table 1 in Ref. [12]). Furthermore, many countries have not adapted their border policies consistently. Thus, travel health practitioners find themselves in a conflicting situation between current WHO recommendations and official country regulations, further complicated by constantly changing country-specific entry requirements. Currently, if in doubt, YFV is often administered rather than risking the traveller being denied entry into a country. However, it is assumed that all countries will respect the new recommendations of lifelong protection after YFV in due time.

Table 1: Case descriptions and results from the yellow fever vaccination survey among Swiss tropical and travel health experts.

	Sufficient yellow fever vaccine available				**Yellow fever vaccine shortage**			
	Overall n	**Vaccinate** n (%)	**Not vaccinate** n (%)	**Exemption** n (%)	**Overall** n	**Vaccinate** n (%)	**Not vaccinate** n (%)	**Exemption** n (%)
Cases 1 and 2: Couple travelling to South-East Zambia and returning to Switzerland via South Africa. While the 62-year-old wife flies back directly (transiting only in Johannesburg), her 63-year-old husband stays for three more days in Johannesburg. Both never vaccinated against YF.								
Wife	38	14 (36.8)	**23 (60.5)**	1 (2.6)	34	2 (5.9)	**20 (58.8)**	12 (35.3)
Husband	40	**35 (87.5)**	3 (7.5)	2 (5.0)	34	7 (20.6)	4 (11.8)	**23 (67.7)**
Case 3: 27-year-old woman, 15th week of pregnancy, travelling to Rio, São Paolo and for 3 days to Iguaçu. Never vaccinated against YF.								
	43	2 (4.7)	**26 (60.5)**	15 (34.9)	33	1 (3.0)	**20 (60.6)**	12 (36.4)
Case 4: 31-year-old woman, 23rd week of pregnancy, travelling to Cameroon. Never vaccinated against YF.								
	40	**17 (42.5)**	2 (5.0)	21 (52.5)	33	**13 (39.4)**	–	20 (60.6)
Case 5: 35-year-old man, travelling three weeks to Peru (Lima, Cuzco, Machu Picchu) and Bolivia (La Paz, Cochabamba), then directly for 2 weeks to Thailand. Never vaccinated against YF.								
	42	**38 (90.5)**	2 (4.8)	2 (4.8)	38	14 (36.8)	5 (13.2)	**19 (50.0)**
Case 6: 30-year-old woman, travelling three weeks to Ghana for scientific studies with fieldwork. She suffers from Crohn's disease and is treated with azathioprine/6–mercaptopurine. Never vaccinated against YF.								
	39	8 (20.5)	**4 (10.3)**	27 (69.2)	31	7 (22.6)	**1 (3.2)**	23 (74.2)
Case 7: 59-year-old man, travelling to Uganda and Ethiopia for three weeks. Because of a polycythaemia he is treated with the cytostatic agent hydroxicarbamide. Received a documented YF vaccination in 1999.								
	42	4 (9.5)	12 (28.6)	**26 (61.9)**	34	2 (5.9)	9 (26.5)	**23 (67.7)**
Case 8: 65-year-old man, travelling to Kenya for a visit to the Maasai Mara National Reserve. Received a documented YF vaccination in 1973.								
	43	8 (18.6)	**34 (79.1)**	1 (2.3)	35	1 (2.9)	**31 (88.6)**	3 (8.6)

YF = yellow fever
Swiss travel vaccination recommendations of October 2013 [1] are in **bold type**.

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