Travel Medicine and Infectious Disease 52 (2023) 102561

Contents lists available at ScienceDirect

Travel Medicine and Infectious Disease

journal homepage: www.elsevier.com/locate/tmaid

Comment on: "New recommendation on yellow fever booster vaccination in Germany"

To The Editor

We thank Schaumburg et al. [1] for their interest in the new recommendation on yellow fever (YF) booster vaccination in Germany and in our systematic review that led to the modified recommendation by the STIKO (German Standing Committee on Vaccination) [2,3]. However, their criticism cannot go unchallenged.

Duration of protection after a single dose of YF vaccine has been discussed for decades. After the World Health Organization (WHO) decision in 2013 to stop routine booster vaccinations, there have been doubts about the lifelong protection by a single vaccine dose [4–6]. Although YF vaccination has been available since the 1930s, strong evidence on the duration of protection is still lacking. This holds particularly true for long-term protection and vaccine effectiveness and safety in groups with a potentially reduced immune response such as small children, pregnant women and persons with primary or acquired immune deficiency. Therefore, many countries inside and outside Europe decided to continue booster vaccination against YF, e.g., the United States, Canada, Austria, France, the Netherlands, and the United Kingdom.

While the WHO represents a public health perspective that focuses on recommendations for people living in endemic countries, the STIKO gives advice on vaccination for individuals travelling from Germany to YF endemic areas.

The new STIKO recommendation for YF booster is based on a systematic review that included all currently available literature. We decided to exclude retrospective studies as the reliability of these studies is much lower than that of prospective studies. Retrospective studies are mostly based on patient self-reporting of YF vaccination(s). The vaccines might have been administered decades ago and it is possible that only some of the received doses were remembered. In contrast, in the included prospective studies a baseline antibody titer was often determined and vaccinations were routinely documented, e.g., as part of a clinical study, which leads to higher reliability (https://www.cebm.ox.ac.uk/resources/levels-of-evidence/oxford-centre-for-evidence-based-medicine-levels-of-evidence-march-2009).

Due to the data available, the focus of our systematic review was on humoral immunity. A titer >1:10 in the plaque reduction neutralization test (PRNT) is currently used as a correlate of protection by WHO. YF vaccination leads to the formation of memory B cells. There is no comparable correlate for T cell-mediated protection following YF vaccination. This results from the fact that so far, only a limited number of studies has examined the protective role of T cell immunity in response to YF vaccination, notably the activation of $CD4^+$ type 1 T helper cells and of $CD8^+$ cytotoxic T cells. We discussed several manuscripts on T cell immunity in our scientific background article [3]. Our conclusion is that the exact role of T cell immunity in the protection against YF is currently unclear. In fact, the protective function of YF-specific memory T cells has been questioned by elegant experiments with chimeric viruses [6].

In their correspondence, Schaumburg et al. argue that a booster vaccination against YF is not necessary, because the number of YF cases among German travellers has not increased since the discontinuation of the booster. In this context, it is important to emphasize that only a low number of YF cases has been reported amongst German travellers in general and that only few travellers exist who have not received an YF vaccine booster during the past decade. Interestingly, in 2013, Grobusch et al. reached a conclusion similar to ours: "The lack of documented vaccine failures in travellers who have been vaccinated against YF virus can be explained by the rarity of YF in travellers in general and does not exclude the possibility of waning immunity." [4]. Clearly, YF cases in vaccinated individuals have previously been reported and recently seen during the YF outbreaks in Brazil in 2016/2017 and 2017/2018.

The WHO recommendation for the use of fractionated YF vaccine doses is currently limited to emergency situations in the context of a YF outbreak (https://www.who.int/publications/i/item/WHO-YF-SAGE-16-1). No country is recommending fractionated YF vaccine doses for travellers. Although the first results on the efficacy of fractionated vaccine doses are encouraging [7], further studies (e.g., on the duration of protection) are needed before implementing fractionated YF vaccine doses as a routine procedure. We consider research in this area as highly relevant and would like to see studies comparing full versus fractionated YF vaccine doses.

Funding sources

None

Dwclaration of competing interest

None to declare

References

[1] Schaumburg F, Schuler F, Grobusch MP. New recommendation on yellow fever booster vaccination in Germany. Trav Med Infect Dis 2022;50:102487.
[2] Kling K, Domingo C, Bogdan C, Duffy S, Harder T, Howick J, et al. Duration of protection after vaccination against yellow fever - systematic review and meta-analysis. Clin Infect Dis 2022;75(12):2266–74.
[3] Kling K, Bogdan C, Domingo C, Harder T, Ledig T, Meerpohl J, et al. STIKO-Empfehlung zur Gelbfieber-Auffrischimpfung vor Reisen in Endemiegebiete und für exponiertes Laborpersonal. Epidemiol Bull 2022;32:3–35.
[4] Grobusch MP, Goorhuis A, Wieten RW, Verberk JDM, Jonker EFF, van Genderen PJJ, et al. Yellow fever revaccination guidelines change – a decision too feverish? Clin Microbiol Infection 2013;19(10):885–6.
[5] Plotkin SA. Ten yearly yellow fever booster vaccinations may still be justified. J Trav Med 2018;25(1).
[6] 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.

https://doi.org/10.1016/j.tmaid.2023.102561
Received 30 January 2023; Received in revised form 8 February 2023; Accepted 2 March 2023
Available online 24 March 2023

[7] Juan-Giner A, Kimathi D, Grantz KH, Hamaluba M, Kazooba P, Njuguna P, et al. Immunogenicity and safety of fractional doses of yellow fever vaccines: a randomised, double-blind, non-inferiority trial. Lancet 2021;397(10269):119–27.

Kerstin Kling*
Immunization Unit, Department of Infectious Disease Epidemiology, Robert Koch Institute, Berlin, Germany

Cristina Domingo
Center for International Health Protection, Robert Koch Institute, Berlin, Germany

Christian Bogdan
Mikrobiologisches Institut – Klinische Mikrobiologie, Immunologie und Hygiene, Friedrich-Alexander-Universität (FAU) Erlangen-Nürnberg and Universitätsklinikum Erlangen, Erlangen, Germany

Medical Immunology Campus Erlangen, FAU Erlangen-Nürnberg, Erlangen, Germany

Thomas Mertens
Institut für Virologie, Universität Ulm und Universitätsklinikum, Ulm, Germany

Robert Wolff
Kleijnen Systematic Reviews Ltd, York, United Kingdom

Ursula Wiedermann
Institut für Spezifische Prophylaxe und Tropenmedizin, Medizinische Universität Wien, Wien, Austria

* Corresponding author.
E-mail address: klingk@rki.de (K. Kling).