

Master Thesis

Master of International Health (MIH)

**Assessment of Immunogenicity and Safety of Yellow  
Fever Vaccination in HIV-infected Patients**

- A Pilot Study -

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## 1 Summary

**Introduction:** Yellow fever (YF) is an acute haemorrhagic fever with a case fatality rate of 15-50 percent. It can effectively be prevented by the administration of a live-attenuated 17D yellow fever vaccine. Little is known about immunogenicity and safety of yellow fever vaccination in HIV- infected patients. Since outbreaks occur in HIV epidemic countries, especially in sub-Saharan Africa, and an increased proportion of HIV- infected travellers to YF epidemic countries has been observed, YF vaccination in HIV- infected patients has become a serious public health concern. To assess immunogenicity and safety of YF vaccination in HIV- infected patients, a retrospective pilot study was performed in 94 HIV- infected patients of the Swiss HIV Cohort Study (SHCS), which took place at the HIV-outpatient clinic of the University Hospital of Bern.

**Methods:** Using the “travel to tropical countries” tag of the SHCS database (timeframe January 1<sup>st</sup>, 1996 until 31<sup>st</sup> of August, 2005), 317 HIV- infected travellers and an additional 13 SHCS participants enrolled by clinical consultations, were identified and asked about their travel destinations and whether they received YF vaccination. Using the plaque reduction neutralisation test, analysis of YF neutralisation titre (NT) was done by M. Niedrig at the Robert Koch Institute in Berlin, Germany, at least once per patient and up to four times for the follow up. NT of  $\geq 1:10$  were defined as reactive and  $< 1:10$  as non- reactive. NT results of tested individuals were tabulated for 1 year post vaccination (1 YPV),  $>1-10$  YPV and  $> 10$  YPV. The results were compared to the YF vaccinated non- HIV- infected individuals from the study of Niedrig et al.<sup>1</sup> Serious adverse vaccination reaction (SAVR) was defined by hospitalisation within 6 weeks after vaccination. All patients’ characteristics were taken from the SHCS database.

**Results:** Of the 330 HIV-infected travellers, 257 patients (78%) were asked about their travel destinations and received YF vaccination. A total of 140/257 patients (55%) travelled to YF endemic countries; 94 of which were documented for YF vaccination. Of these 94 HIV- infected patients, 42 patients (45%) were YF vaccinated before (group 0) and 52 patients (55%) after HIV- diagnosis (group 1). In group 1, in 46/52 patients NT could be performed within one year post vaccination (YPV) (median 3.2 months), demonstrating that 36 patients (80%) revealed reactive NT, while 10 patients (20%) showed non-reactive NT. This was significantly less ( $p= 0.003$ ) than in non- HIV- infected individuals, in whom 64 patients (97%) revealed reactive NT in the first YPV. The NT in the first YPV was significantly lower ( $p= <0.0001$ ) in HIV- infected (median NT 1:22) compared to non- HIV- infected individuals (median NT 1:75). In 6 patients, who revealed reactive NT in 1YPV and in whom follow-up titres were available, non- reactive NT were demonstrated after a median of 2.05 years. In group 0, in the first YPV, all of the 6 patients produced reactive NT. In the timeframe  $>1-10$  YPV (median 5.7 years), reactive NT was found in 21 patients (68%) and non-reactive NT was detected in 10 patients (32%). In a linear regression model, including CD4 cell counts and plasma HIV RNA, NT in the first YPV was significantly associated with undetectable plasma HIV RNA (coefficient 34.0; 95% CI 4.4 – 63.6;  $p= 0.025$ ). Age, sex, CD4 cell count, CD4 cell nadir, taking high antiretroviral therapy, HCV- co-infection, smoking habits or other live vaccines administered at the time of YF vaccination, were not associated with an impaired YF immune response. However, this might be due to the small sample size of this pilot study. An ongoing multi-centre study will analyse these parameters with a larger sample size. No SARV to YF vaccination was found in HIV- infected patients.

**Conclusion:** HIV-infected patients develop significantly less and lower reactive NT to YF vaccination in the first year post vaccination than non- HIV- infected individuals and there may be a faster decline of NT in HIV- infected patients in the latter years. In addition, undetectable viral load might be associated with better serologic response. For primary assessment of immune response, NT detection one month until one year post YF vaccination should be performed. In case of potential exposure, NT detection should be performed respectively a booster should be evaluated 2-5 years post primary YF vaccination.