Measurement of yellow fever vaccine efficacy; is 10 years the right point in time for revaccination?

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Objectives:1) By measuring neutralising antibodies as well as immune memory in travelers vaccinatedpreviously (> 10 years ago) with yellow fever vaccine, an assessment of the duration ofvaccine induced immunity can be made.2) To provide the basis...

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Viral infectious disorders
Study type	Observational invasive

Summary

ID

NL-OMON39667

Source
ToetsingOnline

Brief title
YETI 10

Condition

- Viral infectious disorders

Synonym
Yellow fever infection

Research involving
Human

Sponsors and support

Primary sponsor: Academisch Medisch Centrum
Source(s) of monetary or material Support: Ministerie van OC&W

Intervention

Keyword: Duration, Protection, Yellow fever vaccination

Outcome measures

Primary outcome

The primary outcome measure is the proportion of volunteers who have 0.7 log10

plaque

reduction, as challenge experiments have shown this to correlate with

protection.

Secondary outcome

Another outcome measure is the proportion of volunteers who have YF-17D-specific

memory, as shown by the presence of YF-17D-specific cytokine producing CD8+ and

CD4+ T cells.

Study description

Background summary

The yellow fever vaccine (17D strain) has been in use since 1937 when it was used in a mass vaccination campaign in Brazil [1]. In travel medicine, it is administered to travelers visiting endemic countries or countries where vaccine is required [2] namely South American and African countries.
According to international health regulations, vaccines need to be re-administered every 10 years [3]. The regulation is conservative, since vaccine immunity appears to last several decades if not for life. Previous studies have already provided a base of this evidence by showing that neutralizing antibodies persist in vaccinated persons for many more years [4, 5].
Neutralizing antibodies have long been thought to be the primary protection

against the
Yellow fever virus [6]. Recent findings have indicated that the innate as well as the CD8 T
cell response might also be important aspects in the immunologic protection. It has been
shown that highly polyfunctional memory CD8+ T cells are elicited and maintained, for years
after vaccination [7]. Probably, the responses of these cells are also important in the long-term
immunologic protection against yellow fever virus.
With this study we aim to add to the knowledge about the long term humoral and cellular
immunity against yellow fever vaccination, in order to provide a broader scientific basis on
which guidelines can be improved for vaccination campaigns in endemic areas as well as for
travelers seeking preventive healthcare advice.
In the AMC, around 1300 travelers receive a yellow fever vaccine annually. In around 1 in
every 18 yellow fever vaccine recipients, the yellow fever vaccine is a booster for a
previously administered vaccine.
In order to assess the duration of the immunologic response, we will measure neutralizing
antibodies as well as T cell memory in travelers who attend our pre travel clinic more than 10
years after a primary yellow fever vaccination.
Hypothesis: The duration of yellow fever vaccination protection lasts for over 10 years after
vaccination.

Reference list
1. Smith HH, Penna HA, Paoliello A. Yellow Fever vaccination with cultured virus (17D)
without immune serum. Am J Publ Hlth 18:437, 1938.
2. Manso C, de S. Mass vaccination against yellow fever in Brazil 1937-54. In: Smithburn
KC, et al, eds. Yellow Fever Vaccination. Geneva: WHO, 123-140, 1956.
3. WHO. Revision of the International Health Regulations. 58th World Health Assembly.
WHA 58.3, 2005.
4. Poland JD, Persistance of neutralizing antibody 30-35 years after immunization with 17D
yellow fever vaccine. Bull World Health Organ 59: 895-900, 1981.
5. Bodilis CG, Benebdelmoumen G, Gergely A, et al. [Long term persistence of yellow fever
neutralising antibodies in elderly persons]. Bull Soc Pathol Exot 104:260-265,

2011.
6. Mason RA, Tauraso NM, Spretzel RO, et al. Yellow fever vaccine: direct challenge of
monkeys given graded doses of 17D vaccine. Appl Microbiol 25:539, 1973.
7. Akondy RS, Monson ND, Miller JD, et al. The Yellow Fever virus vaccine induces a broad
and polyfunctional human memory CD8+ T cell response. J Immunol., 183: 7919-7930, 2009.

Study objective

Objectives:
1) By measuring neutralising antibodies as well as immune memory in travelers vaccinated
previously (> 10 years ago) with yellow fever vaccine, an assessment of the duration of
vaccine induced immunity can be made.
2) To provide the basis for considering a longer time period before revaccination is
considered necessary with the current vaccine.

Study design

Trans sectional study including all travelers at the pre-travel clinic who have been administered a
yellow fever vaccination > 10 years ago. All volunteers shall be asked to give their informed
consent. Blood samples shall be drawn before new vaccinations are administered, to
measure neutralizing antibodies and to measure T cell memory.
Of the group with no neutralizing antibodies, all volunteers shall be assessed for the presence
of T cell memory. In the group with neutralizing antibodies, a random sample (~32/105, 31%)
shall be analysed for the presence of T cell memory.

Study burden and risks

n.a.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)
Elderly (65 years and older)

Inclusion criteria

> 18 years
having been administered a yellow fever vaccination

Exclusion criteria

< 18 Years
Vaccination administered < 10 years prior

Study design

Design

Study type: Observational invasive

Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Prevention

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	22-03-2013
Enrollment:	119
Type:	Actual

Ethics review

Approved WMO Date:	07-01-2013
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	26-03-2013
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	29-05-2013
Application type:	Amendment
Review commission:	METC Amsterdam UMC

Study registrations

Followed up by the following (possibly more current) registration

No registrations found.

Other (possibly less up-to-date) registrations in this register

No registrations found.

In other registers

Register	ID
CCMO	NL41264.018.12