

SCIENTIFIC STUDY GROUP ON TRAVEL MEDICINE
WETENSCHAPPELIJKE STUDIEGROEP REISGENEESKUNDE/GROUPE D'ETUDE SCIENTIFIQUE DE LA MEDECINE DES VOYAGES
NATIONAL CONSENSUS MEETING

Brussels, June 26th, 2015

Presided by Fons Van Gompel and Yves Van Laethem
Report by Patrick Lacor and Fons Van Gompel - draft 02/10/2015

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INTRODUCTION.

Yves Van Laethem opens the meeting by thanking all the participants for being present and taking part in the discussions on which the consensus will be based. In particular, he thanks Fons Van Gompel for being the driving force behind all this.

Fons Van Gompel emphasizes that the goal of this meeting is to give a concise updated overview of the most important topics -and to discuss more in detail those topics that need to be fine-tuned- but NOT to give an exhaustive review of travel medicine in 2015.

The national consensus is based on data and guidelines provided by WHO, MEDASSO and CDC and the scientific literature of the foregoing 12 months

The accompanying SLIDES of this consensus document (pdf-version of the PowerPoints) & the consensus BROCHURE (in Dutch and French) are highlighting these issues and the proposals for changes. They will be available on the website of the ITM, and may be used for teaching purposes.

Fons Van Gompel and also draws attention to the upcoming national seminar on travel medicine, organized every 2 years since 1995, and that will take place in November 19th, 2015.

SUMMARY OF THE CONSENSUS DISCUSSION.

YELLOW FEVER

The scientific WHO statement of May 2013 **“one injection of the yellow fever vaccine will offer a lifelong protection, hence the validity of the proof of vaccination is lifelong”** has been published again in the July 2015 adaptation of the WHO-ITH book.

The WHO published a very practical list : <http://www.who.int/ith/2015-ith-annex1.pdf?ua=1>.

Some countries already agree with this May 2013 statement; amongst the countries with risk of yellow fever : Angola, Cameroon, Congo-Brazzaville (but not the *Democratic Republic of Congo*), Ghana, Soudan, Ecuador, British Guyana & Suriname (but not *French Guyana*) and Paraguay.

The WHO **“yellow fever maps”** makes a distinction between

- the “lightly” colored countries = countries with “very low to negligible risk” of YF
 - the “red” colored countries = countries where YF vaccine is (strongly) recommended or even obligatory
- Rwanda becomes “lightly colored”; Democratic Republic of Congo is now entirely “red colored” again.

It can be assumed that **South Africa** will maintain a requirement of YF vaccination for travelers coming from “red colored countries”, although in February 2015, it agreed explicitly NOT anymore to require a vaccination certificate for travelers coming from the “lightly colored countries” Zambia, Tanzania, Eritrea, Somalia and São Tomé. For travelers with a “transit stay” in Ethiopia, YF vaccination would best be recommended, independently of the transit duration, as an unforeseen prolongation of transit time above 12 hours is always possible. Although South Africa will not provoke anymore difficulties for travelers

coming from Zambia, **other countries in that region** will probably continue to do so, as we learned recently : people who walked over the bridge from Zambia tot the Zimbabwean side of the Victoria Falls were in difficulty because of no proof of vaccination – this is ridiculous, but regrettably the truth. So, probably also Namibia and Botswana can be demonstrate a nasty compoment at their borders ? For details see <http://www.who.int/ith/2015-ith-annex1.pdf?ua=1> (and <http://www.who.int/ith/2015-ith-county-list.pdf?ua=1>)

NB. What about the “cholera stamp” in the yellow-fever-booklet (“*cholera vaccine not indicated – validity indefinitely*”) ? The habit of putting it on the vaccination certificate or travelers to sub-Saharan Africa should be maintained. Never needed for other regions in the world.

Can it be stated that YF vaccine offers a lifelong protection with one injection in everybody ?

This question is particularly delicate when it concerns the primovaccination of **“slightly” immune depressed hosts, or a child in the age category 6m – 2 years, or persons older than 60 years, or pregnant women**. The WHO does not give a definite answer, only stating that “further research is needed”. Also in the algorithm in the UK Green Book 2014 the recommendation for revaccination is rather vague. The US CDC / ACIP 2015 guidelines (MMWR June 19 2015) recommend to revaccinate pregnant women, persons that underwent stem cell transplantation, and people with hiv-seropositivity at the moment of the first dose. It is clear that this “uncertainty” is a difficulty to handle with when **informing travelers**. So what should be our vaccination strategy when confronted with a “slightly immune depressed” host, etc. ? Can we say that one injection offers a lifelong protection? Should we recommend a booster after 10 years? Or should we revaccinate e.g. the child once it is older than 2 years?

What makes it especially difficult is that we are assumed to add a “validity period” to the vaccination certificate. We could skip the addition of an “end date”. Or we could write down that protection will have a duration of “at least 10 years”. Or, we could add a “Post-it” note (or **sticky note or stapled note**) to the certificate as a reminder to the vaccinated person that a booster should be reconsidered at the occasion of a future trip. After all, if we write down a “waiver” for a “definitely” immunocompromised host, we also add an end date; so why not do the same in “uncertain situations”?

In summary, we can say that at this moment, there is controversy concerning the duration of the protective effect of YF vaccine in certain categories of travelers. One YF vaccine will surely give them protection but the duration of the protective effect is probably variable and depends on the immune condition of the vaccinated person. The vaccinated person should understand that there is a “grey zone” and that an “individually tailored” decision has to be made. The question of (already) giving a booster yes or no should then be dealt with at the occasion of future travel plans.

Should **old age category** still be taken into consideration as a precaution (not the same as contra-indication) ? Of course, although the incidence of severe adverse reactions (YEL-AND and YEL-AVD) is very to extremely low. There was a recent case report of a 60 years old American female that died after YF vaccination. Post mortem analyses revealed however that she had a thymoma (and positivity for anti-acetylcholinesterase antibodies) but still, it should make us realize that the vaccine is not without danger (in this age category).

We need to stay vigilant. In case of a feverish syndrome related to YF vaccination, a serum sample should be sent to the Robert Koch Institute in Germany.

What about the immune suppressed host?

We refer to the article of W. Peetermans et al (Tijdschrift voor Geneeskunde 2013; 69(2): 1113-1116) that proposes time intervals to be respected after discontinuation of immune suppressive drugs.

What if two live attenuated vaccines are indicated (YF and MMR)?

The “classical” recommendation is to give them both together on the same day, **or** separated with an interval of 28-30 days. Although the data in the literature are somewhat controversial, vaccine

administration with an interval of 30 days (in the Netherlands > 21 days) is preferable as this would lead in general to a higher seroconversion rate. Only if that is not possible, vaccine administration together on the same day is advised.

The 2015 French guidelines (BEH June 2015) says that "any interval will do if a 30 days interval is not possible" (which is supported by a recent publication in Vaccine)

MALARIA

In the past, when WHO skipped the labels "A, B, C and D" and introduced the zones "I,II,III,IV" to indicate the malaria regions worldwide, we continued using the letters A and C (skipping the letter B when proguanil was not available anymore).

In 2014 however, WHO re-introduced again the labels A, B, C and D for the different malaria-zones.

- B= Risk for P vivax malaria only
- Importantly they introduced a footnote : alternatively, when travelling to rural areas with low risk of malaria infection, mosquito bite prevention ..can be combined with ..stand-by emergency treatment (SBET)

We have to be careful when giving a "low malaria risk" score to certain regions: fever occurring after a stay in a region with a "low risk label" can still be caused by malaria. An important message to be given is that mosquito protection is always indicated AND that if fever occurs, malaria should always be considered in the differential diagnosis. But, when traveling in a "low risk area" then the option can be chosen to apply anti-mosquito measures only, and to use SBET (standby emergency treatment) in case of suspicion of acute malaria.

Another possible scenario is that of the traveler crossing countries/areas with varying risk of malaria.

In that case, it could be decided to only start chemoprophylaxis when entering a zone of "higher" risk, avoiding to be on antimalarials for long periods of time when it is really not necessary nor useful.

This could thus be considered a kind of "stand-by" or "on-demand" chemoprophylaxis", but this is a rather confusing term. So how should we call this type of treatment? Amongst the many proposals "on demand regional risk based malaria chemoprophylaxis seem to suit best (realizing that "on demand" in English is not entirely the same as the French "à la demande", hence the addition of the notion "regional risk based", what supposes that the information on the website permits judgement in this matter.

We should reflect on this, but finally decide at the end of October 2015.

Anyway, the traveler carrying "treatment in the pocket" will probably continuously be reminded of the potential risk, and thus behave accordingly. In that way, the principle of prescribing antimalarials as SBET or "risk-based on demand" represents a contribution to effective ABCD-prevention (WHO : Awareness, antiBite, Chemoprophylaxis, rapid Diagnosis).

Malaria prophylaxis indeed is a matter of "shared informed decision", a subject to be thoroughly discussed with the individual traveler. **Voumard et al** : "When travelling to moderate- to low-risk malaria areas, 85% of interviewees chose not to take chemoprophylaxis as malaria prevention, although most (non-Swiss) guidelines recommend it". ... hence 15 % of interviewees chose to take chemoprophylaxis as malaria prevention, although Swiss guidelines do not recommend it ? ... "New recommendations should include shared decision-making to take into account travellers' preferences."

Malaria-recommendations for Asia & Latin America - proposal:

- In **most** regions in Asia & Latin America (see map of the German-speaking countries <http://www.dtg.org/21.0.html>) one can skip the continuous chemoprophylaxis (even for adventurous travellers) after a thorough evaluation of the (mostly low to very or negligible low) malaria risk depending on the region (& rural or urban) & season, but mostly depending of the type of accommodation.
- Strict measures are to be taken against mosquito bites from dusk till dawn.
- In case of fever occurring after a stay in a region with a "low risk malaria" can rarely still be caused by malaria and needs ,,,,
- In many itineraries with variable malaria-risk (sometimes probably more elevated malaria risk) the "on-

demand (regional risk based) malaria chemoprophylaxis" (information on [www,itg.be](http://www.itg.be)) with Atovaquone/Proguanil and/or "emergency malaria treatment" (& complete instructions) with the same antimalarial are complementary option(s).

The recommendations on the ITM website have not yet been updated, this will be accomplished before the end of the year 2015.

VACCINES

VACCINES AND the risk for ANAPHYLAXIS

Anaphylaxis following administration of a vaccine (after excluding severe allergy by medical history) is extremely rare. Still, 15' of observation (in the waiting room or in the hall of the travel clinic) is a safety rule after vaccination.

<http://tinyurl.com/HGR-8802-anafylaxie> & <http://tinyurl.com/CSS-8802-anaphylaxie>

BOOSTRIX

There is a recommendation made by the HGR/CSS in 2013 : if someone is in need of a tetanus vaccine booster, then once TDaP should be used. BOOSTRIX POLIO is also available (but somewhat more costly).

POLIOMYELITIS

One booster in adulthood ($\geq 16y$) provides lifelong protection against the disease, if complete primary vaccination schedule has been administered.

WHO is nowadays especially concerned with the risk of re-importation by (healthy) carriers of the virus in polio-free countries.

WHO will update every 3 months the actual status of "still exporting currently" and "not currently exporting" countries. The website of ITG will be updated accordingly.

TYPHOID FEVER

There is a fluctuating shortness of Typhim Vi at this moment. Although Typherix is intermittently available for the travel clinics, in pharmacy it may be not easy to obtain. Vivotif is not available.

The recommendation in Belgium "*that the vaccine is recommended in case of a trip to the tropics of more than 3 weeks duration, but less than 3 weeks if the trip is adventurous*" has not been changed the last 15 years, but it is time to restrict a bit more the indications, as the risk for the traveler has changed in the last decade.

Or, we can state as a double "one liner"

- vaccination against typhoid fever is **especially indicated** in case of an adventurous trip in **poor sanitary conditions** to **tropical or subtropical countries**.
- vaccination against typhoid fever **can be considered** in case of a trip to tropical or subtropical countries of **longer than 3 weeks** duration (**especially for trips to the Indian subcontinent**)

NB the **CATMAT** 2014 recommendations are stating that it is only indicated for South Asia = the Indian subcontinent.

MENINGOCOCCAL MENINGITIS

The risk is declining as in "risk countries" in the meningitis belt, the multivalent vaccine is now more and more used. The indications for the vaccination are not changing.

RABIES

No changes so far. In case of short notice travel, an accelerated schedule can be used .

Patrick Soentjens will talk about it at the seminar in November 2015.

JAPANESE ENCEPHALITIS

An **accelerated Ixiaro schedule** has now officially been proposed by the EMA, namely at day 0 and day 7 (instead of day 28), booster after 12-24 months – only for adults 18-65 y - but with the precaution to have both doses at least 7 days before departure.

How long does immune protection last after 3 X Ixiaro ? There are data now stating that the duration of protection is 6 to 10 years.

The vaccine is certainly indicated for expats.

Alternative for vaccination : mosquito protection should be applied when dusk starts (as *Culex* behaves somewhat different than *Anopheles* who starts biting mostly on a later moment).

Apart from the inactivated vaccine (Ixiaro), there is also an Australian & Chinese **live attenuated vaccine** with good effectiveness after 1 injection. Vaccination "on site" could thus be considered for expats. Will 1 injection live attenuated vaccine suffice? the answer in the literature is mostly yes, however, the data have to be interpreted carefully as they mostly apply to people chronically exposed to JE (and possibly other Arboviruses).

TICK BORNE ENCEPHALITIS

The serological response is thought to persist very long after the first booster dose.

NEARBY TRAVELS

This is a new topic that was put on the ITM website, in which a map is used (shown on slide).

TRAVELERS' DIARRHEA

The "Belgian algorithm" includes the option of "self treatment".

There is a recent review by Robert Steffen (JAMA 2015; 313(1): 71-80).

The phenomenon of ESBL colonization after travel is well known. However, it is not clear how this translates to prophylaxis. (See also the Kantele article: CID 2015; 60: 837-46).

Dr. Lucie Seyler will handle the topic at the November 2015 seminar.

CHIKUNGUNYA, DENGUE

No special news. (shown on slide).

A dengue vaccine is in far advanced stage (shown on slide).

HAJJ

Saudi-Arabia made the recommendation not to do the Hajj for people with underlying diseases at this moment, taking into account the MERS-CoV risk.

The recommendations did not change since 2014.

At the moment of this writing, the Hajj is ongoing - near the end.

EBOLA

Travel advice will be according to the further evolution of the epidemic.

At the moment of this writing, the epidemic is near the end.