

SCIENTIFIC STUDY GROUP ON TRAVEL MEDICINE

WETENSCHAPPELIJKE STUDIEGROEP REISGENEESKUNDE/GROUPE D'ETUDE SCIENTIFIQUE DE LA MEDECINE DES VOYAGES

NATIONAL CONSENSUS MEETING 2017

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Presided by Ula Maniewski-Kelner and Patrick Soentjens

Report by Rembert Mertens

INTRODUCTION.

Ula Maniewski opens the session (which will be audio-recorded) by thanking all participants for being present, and encourages the audience to participate at the discussions between the different presentations.

The two main topics that will be addressed today are the adaptation on the Belgian guidelines concerning yellow fever vaccination, and the organization of post-exposure prophylaxis for rabies in Belgium by the ITM in Antwerp.

Patrick Soentjens informed the audience of the upcoming 10th European congress of tropical medicine and international health (ECTMIH 2017). ECTMIH is a biennial event under the auspices of the Federation of European Societies of Tropical Medicine and International Health (FESTMIH). It will be organized in Antwerp from 16-20 October.

Also he invited the audience for participation on the National Seminar on Travel Medicine (organized every 2 years since 1995) and that will take place the 25th of January 2018.

CONSENSUS DISCUSSION.

YELLOW FEVER

As of 11-07-2016 no booster dose or revaccination against yellow fever is required anymore, as a condition of entry into a country, regardless of the date on which the initial dose was administered. There were no specific recommendations made by WHO on possible suboptimal protection in subpopulations, and each country was to decide, in its own guidelines, if and when a booster dose could be offered to certain patients. As a consequence, there were many differences in the different national guidelines worldwide since then.

Review of data from Brazil (dating from 1973-2008), published in 2013, concerning sylvatic yellow fever and possible failed vaccination (reported in that specific publication: in more than 50% of clinical cases of YF), as well as questions regarding the duration of immunity after YF vaccination (especially in non-endemic countries), raised concerns concerning the statement by WHO in July 2015 that one injection of the vaccine offered life long-protection. Also the suggested protective role of cellular immunity was disputed.

Before making new changes to the Belgian guidelines of 2016, the study group looked at the available literature, and compared the different national guidelines (CDC, UK-NaTHNaC, Dutch and French guidelines, and the Swiss-ECTM).

Although the Swiss guidelines seemed the most straightforward, those guidelines are quite in contradiction to the recommendations made by WHO in 2015, as they offer a (single) booster dose after ten years, to every traveler visiting a country where yellow fever is endemic.

The Belgian guidelines on yellow fever vaccination were updated as follows :

- booster vaccination is offered to children vaccinated before the age of 24 months (2016 guideline stated 9 months)

- a single booster (when primary vaccination was given more than ten years earlier) is offered in case of "high risk of exposure" (eg labo workers handling wild type yellow fever, staying for extended period in endemic region or travelling to high risk region such as rural Western Africa or an epidemic region).

(2016 guideline stated lab workers, or persons travelling to an area with an outbreak of yellow fever)

- depending on the urgency of the decision to revaccinate or not, testing of neutralizing antibodies against yellow fever can be suggested before deciding to administer a booster dose.

No changes were suggested concerning the administrative part ("lifelong" for the majority of vaccinated travelers, "1year" in specific situations eg. pregnancy, children < 24 months, "10 years" in immunocompromised eg. hiv-infection)

In regard with the statement that a booster dose could be offered to travelers at higher risk because of extended stay, or travelers to high risk regions, Ula admitted that this could seem to many as 'a huge grey zone', but that in real life, many experts already had a low threshold for revaccinating ('a single booster' for immunocompetent, and 'every ten years' for immunocompromised)

At the end of the presentation on yellow fever, Ula presented different cases, asking the audience whether they would or would not offer a booster dose in that specific situation.

There were several reactions concerning presentation of the yellow fever (re)vaccination :

- a person from the audience stated that it would be highly unlikely for patients, who were vaccinated last year and received a yellow booklet stating that they had "lifelong protection", to return to the travel clinic consultation even if they were travelling to a high risk region or for an extended period, because they would assume they are protected for life..
- another stated that maybe we should explain to the patients that there still could be a difference between "administrative lifelong protection" and the fact that in specific situations of prolonged stay or high risk regions a single booster might still be considered.
- another person mentioned the fact that some persons vaccinated against yellow fever, in the setting of temporary withdrawal of immune-suppressive treatment, may have received a yellow booklet stating "lifelong", whereas these persons are not to be considered 'fully immune-competent', and that one should not state "lifelong" in those situations. (NB 2016 and 2017 Belgian guidelines state that in those situations a validity for 10 years is written down in the yellow booklet)
- Ula replied that an ad hoc studygroup from de HGR/ CSS (under the coordination of Patrick Soentjens) is working on recommendations concerning vaccinations including yellow fever vaccination in the setting of immunosuppression.
- another person in the audience raised the question on whether or not to revaccinate people > 65 years ? Until now, we (re-)vaccinate in Belgium subjects up to the age of 70.
- concerning the interval between yellow fever vaccination and other live vaccines, usually the measles vaccination -and particularly most recently with the measles outbreak in Belgium- a remark was made that in many situations we do not have certainty if a measles vaccination was administered in time frame of yellow fever vaccination. Another person replied that we should make more use of data with regard to previous vaccination available at Vaccinnet (Flanders region) or e-vax (region Wallonie-Bruxelles). Here a remark was made that also the travel clinics themselves should do more effort to register the vaccines administered at their consultations on those websites .

MALARIA

The world malaria report 2016 showed a reduction in malaria cases worldwide (except in Venezuela); no indigenous cases were reported in Europe (but in 2017 a few cases have been recorded). There is also an outbreak in Cabo Verde in Praia (capital from Santiago) The 2017 'malaria world map' is available at the website of ITM.

As in 2016, the new map shows 4 levels of risk: 'no risk', 'limited risk' , 'moderate risk' and 'elevated risk'

According to WHO stand-by emergency treatment (SBET) can be considered for travelers (or professionals) who spend many 'short periods' in countries with malaria endemicity, as well as for tourists spending a longer period in a low risk region.

Different treatment options are available nowadays in Belgium (atovaquone-proguanil/Malarone; artemether-lumefantrine/Riamet; dihydroartemisinin-piperaquine/Eurartesim) for treatment of (non-complicated, *falciparum*) malaria.

The first choice of SBET will still be atovaquone/proguanil. Exceptionally Riamet or Eurartesim (ACT, Artemisinin combination therapy) can be suggested as an alternative but are not registered as SBET in Belgium. When those alternative SBET are considered, one should keep in mind that an ECG is warranted to exclude QT prolongation, and that in S.E. Asia resistance against ACT is becoming more problematic. The fact that atovaquone/proguanil can be used as malariaprevention and as SBET is another advantage and its lower price compared to the ACT's as well.

ZIKA

A short overview of the most recent epidemiological data was presented, as well as the differences in clinical presentation in travelers compared to local cases. Many questions remain concerning the risk of microcephaly during pregnancy, which trimester of the pregnancy is most at risk, and the possible differences of congenital transmission in Asia vs the Americas. One is advised to regularly check the ECDC map (via the link on the website of ITG) since this map is updated monthly. Testing (PCR +/- serology, depending on whether the patient was symptomatic, and the timing of the return date) for infection with Zika is recommended for symptomatic travelers returning from endemic regions, as well as for as travelers with a pregnancy wish (or their male partners).

POLIOMYELITIS & MEASLES

One booster vaccination against poliomyelitis, in adulthood, provides lifelong protection. WHO is especially concerned with the risk of re-importation of the virus in polio-free countries.

Travelers (of all ages) to Nigeria, Afghanistan and Pakistan, when staying for more than 4 weeks, are obliged to show proof of (re)vaccination against poliomyelitis *dating from less than 12 months, and at least 4 weeks before the return date*. This has to be documented in the international certificate of vaccination, on the pages reserved for mandatory vaccines. In RD Congo and in Syria vaccine-derived polio virus circulates, with potential risk of international spread; for travelers to these two countries a (re)vaccination is not mandatory by WHO, but the (re)vaccination is highly recommended, for travelers staying for more than 4 weeks.

Regarding the measles outbreak in Europe (with 288 confirmed cases in Belgium) we are reminded to check vaccination status (Measles-Mumps-Rubella / MMR) especially for travelers to eastern Europe (eg. Romania, Ukraine); most patients born before 1970 are considered to be immunized, since measles was highly endemic in Belgium before 1970. Two separate doses (interval minimum 4weeks) of the MMR vaccine offer lifelong protection.

As an attenuated live vaccine, one should of course keep in mind the possible contraindications, and the possible interaction with yellow fever vaccination.

RABIES

The procedure on post-exposure prophylaxis was changed in July 2017: when indicated (depending on the risk category, and origin/species of the animal) immunoglobulines are now available via the ITG/ITM, which serves as the expertise-centre for rabies (no longer via WIV/ISP). Good news is that reimbursement (with limitations) is also possible starting from the 3rd of July 2017.

The ITG/ITM will coordinate the administration (and follow-up) of patients in whom MARIG immunoglobulines were indicated. The procedure on rabies PEP is available at the site of ITG/ITM, as well as the contact phone number ("24/7" expert advice: on weekdays, and during working hours through direct communication with the expert at ITG (03 247 66 66 or 03 247 64 05); during the weekend, or at night/in the evening, one should contact the senior internist at the UZA, 03 821 30 00).

There is no rationale for immunoglobulines when more than seven days have elapsed after the start of rabies vaccination abroad.

In situations where post-exposure vaccination was initiated abroad, without the need for administration of immunoglobulines, as well in situations where PEP was initiated in Belgium without the need for MARIG (schema 1 or schema 2) the follow-up and administration of the vaccines could also be organized by other travel clinics or the general practitioner, if this is deemed more practical for the patient.

Several new vaccination schemes are being investigated in the setting of pre-exposure vaccination, where in the near future it might be possible to use fewer doses, and/or intradermal vaccination. This research is promising; in the future probably the principle 'every dose counts' will be more accepted in clinical practice (instead of the more 'rigid' scheme (0-7-28) we use nowadays); and with those new developments, it is likely that we will less frequently need immunoglobulines in the post-exposure setting.

It is worth mentioning that Belgium is the only country where the efficacy of the post-exposure vaccination is verified through measurement of anti-rabies antibodies (virus neutralization test RFFIT).

