SCIENTIFIC STUDY GROUP ON TRAVEL MEDICINE

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

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Presided by *Patrick Soentjens* and *Ula Maniewski*
Report by *Rembert Mertens*

INTRODUCTION *PATRICK SOENTJENS*

A short presentation of data on the registered consultations in travel clinics in Belgium was given (from 2014-2017). The data clearly shows a steady increase (mostly in Flanders and Brussels) yearly over the last four years; with an absolute increase of more than 8000 consultations in 2017 in Belgium, compared to 2014. Regarding the total number of yellow fever vaccination there is a clear increase in doses of yellow fever vaccination administered in Brussels, which is not seen in Flanders and in Wallonia. It is not reasonable to compare these differences between Brussels, Flanders and the Walloons because of different demographics and different populations visiting the travel clinics, but two obvious conclusions can be drawn of these data. First of all the fact that although WHO changed the recommendation on the need for YF booster vaccination in 07/2016, this did not seem to have or large impact on the demand for YF-vaccination in Belgium afterwards; and secondly, we need to overthink ways to cope with the problems arising from the increase of total consultations over these last four years. In the peak season, all of the travel clinics have to deal with an overload of patients. We clearly need to think on future solutions not only for the increasing demands of consultations, but also on the nature of our travel related medical advice, which will evolve more and more to an individualized health assessment of the traveler.

CONSENSUS DISCUSSION.

Update on occurrence of some infectious diseases worldwide *TINE LERNOUT*

Recent epidemiological data on several infectious diseases and current outbreaks were presented.
In the current ***Ebola outbreak*** (data from 05/2018 until 10/2018) in North-Kivu and Ituru province, DR Congo, 194 cases (and 122 fatalities), have been reported, making it the fourth largest Ebola virus outbreak so far. As response to the outbreak, not only contact tracing started in August 2018, but also preventive vaccination (with the rVSV Ebola vaccine MSD®) which targeted not only health care workers, but also contacts of confirmed cases. Over a period of two months, more than 14.000 vaccines were administered. Nowadays more than 33.000 subjects were vaccinated.

From July 2017 up till February 2018, ***the yellow fever epidemic in Brazil*** counted over 700 confirmed cases, with more than 230 fatalities. Unfortunately these numbers are expected to rise even further since the virus circulates in highly populated states , where vaccination previously was not formally recommended.

As of 2 October 2018, 15 cases in Afghanistan and 4 cases in Pakistan of ***wild type polio virus*** have been detected, and the vaccine derived poliovirus continues to circulate in DR Congo, and has been detected again in Niger, Nigeria, Somalia, and Papua New Guinea.

Madagascar has suffered seasonal epidemics of bubonic ***plague*** since the 1980's, with a large outbreak in 2017 (more than 2000 cases and over 200 deaths). These outbreaks typically arise in the rainy season (from September to April). So far in 2018 (from August till September) 13 cases of plague have been recorded (3 of which were confirmed cases; 2 fatalities).

In August 2018 a Saudi-Arabian resident was diagnosed (laboratory confirmed) with ***MERS - Coronavirus*** infection, in the United Kingdom. Since 2012, over 2200 cases were diagnosed (mainly in the Middle-East); in that time frame 16 cases were reported in the EU (all related to recent travel from the Middle East).

Also in the United Kingdom, two (distinct) cases of imported **Monkeypox** were reported, with recent travel history from Nigeria. Recent updates on the rapid risk assessment for MERS and Monkeypox are available at the site of the European Centre for Disease prevention and Control.

In 2017, ten cases of ***Chikungunya-fever*** were reported in Belgium; when compared to 2015 and 2016, fewer cases were reported from Latin-America and Asia, but more cases seem to be imported from the African continent. The reported cases of ***Dengue-fever*** in Belgium also seem to be less frequently imported from the Americas and South-East Asia than before, but the imported dengue cases from Africa and South Asia are on the rise.

The vast majority (84% between 2015-2016) of imported cases of **malaria** in Belgium are still from Central and West-Africa.

An unusual early start and relatively high number of locally acquired ***West Nile-virus infections*** has been observed (more than 900 reported cases, compared to 200-300 usually) in the European Union. This could potentially result in a high number of cases during the coming winter months.

At the end of the presentation, the fact that this year two cases of ***Tick borne encephalitis*** were diagnosed in Belgium, with 1 possible and 1 probable acquisition in Belgium, was mentioned.

MALARIA *ULA MANIEWSKI*

The new guidelines on malaria prophylaxis, and the new updated 'malaria world map 2018' were presented. Estimating the real risk of malaria for travelers is a time consuming process, where the available data on local epidemiology of malaria (data and maps from WHO) cannot simply be extrapolated to travelers, and differences in guidelines or maps (eg. NathNAC - United Kingdom/NHS, Fit for Travel - NHS/Scotland, Tropimed) have to interpreted when deciding whether or not adapt the Belgian guidelines on malaria prevention. The 'malaria world map' is a useful tool for clinicians in the Belgian travel clinics, and even more detailed information and separate country maps (when available) are annually updated at the site of ITG.

An important difference comparing the new map of 2018 to the older versions, is the fact that we no longer use the classes A, B, C for the advice of the sort of malaria prevention, but that **the risk is stratified in 5 categories**, varying from *'no risk*' to *'very high risk'*. **The 3 different attitudes of prevention: *'mosquito prevention only', 'mosquito bite prevention and chemoprophylaxis / SBET in selected situations'* or *'mosquito bite prevention and chemoprophylaxis'*** are guided by this risk stratification.

The selected situations where the clinician should decide to offer chemoprophylaxis in regions of moderate risk, do not only depend on the travel conditions (such as adventurous travelling with jungle excursions) and the type of *Plasmodium* (*falciparum* or not), but also on the travelers profile, and risk factors for complicated malaria should be taken into account, such as age (elderly >70 or travelling with infants or small children), pregnancy, or medical conditions (immunosuppression, co-morbidity, splenic dysfunction or anatomical asplenia).

For countries where the malaria risk varies highly between different regions, or where malaria cases are situated in 'malaria hot spots', we advise to check at the site of ITG for recent country-specific updates, or to check the specific country map (when available), to guide your decision on malaria prophylaxis.

RABIES *PATRICK SOENTJENS*

Retrospective data (from 07/2017 to 06/2018) of **post-exposure prophylaxis against rabies** were presented. Only subjects that received Human Rabies Immunoglobulin (HRIG) were included in the analysis. Seventy-five patients were included in the analysis. The data showed a female predominance of patients (58%) and a low percentage of patients having received Rabies PrEP (4%). Most of the travelers who received this schedule of rabies PEP visited Asia (35%), and the most common bites were canine (36%), or caused by monkeys (25%), and bats (23%). 84% of subjects finalized their vaccine schedule, which showed good compliance. The serological response following PEP was very good for bat bites, and moderate for the other types of exposure (like dog-related injuries).

As presented earlier this year, recommendation on **rabies pre-exposure prophylaxis** (PrEP) was changed in Belgium (this was implemented from the 1st of May 2018), in accordance with the WHO guidelines (published in the Weekly Epidemiological Record in April 2018).
The first-line rabies PrEP regimens (for all ages) are the following two-visit schedules:
- ID: 2x 0,1 ml in 2 different sites on day 0 and day 7 (= 4 injections in total)
- IM: 1 vial of 1.0 ml day 0 and day 7
After completion of the two doses, we suggest the clinician to add a comment - stamp preferred - in the yellow booklet, stating ***"RABIES PrEP completed, additional vaccines needed after bite / risk"***.
Of course this two-visit regimen, with a (minimum) interval of one week, offers a great advantage for patients, and has probably lowered the threshold to decide to vaccinate against rabies for many clinicians. This led to more use of the vaccine - a vaccine for which the stock-problem already seemed to be a never-ending-story. Of course the intradermal route of vaccination offers a solution for the increased demand for rabies vaccines, but due to practical concerns, so far intradermal vaccination is only performed at the ITG and the Belgian Armed Forces. Hopefully the increasing number of travelers receiving PrEP for rabies will lead to a decreased demand for (human) rabies immunoglobulines in the future...

The new WHO guidelines on rabies also implied a **revision of the Belgian guidelines on Post-exposure prophylaxis -PEP- for rabies**. The adapted Belgian guidelines, will be available at the site of ITG from jan 2019.
In centers with sufficient experience with the intradermal vaccination, this route of administration is an option, even in the setting of PEP. Otherwise intramuscular vaccination is still the preferred technique.
The study group agreed to add to **"Schema 1 - subjects with previous PrEP - or - simplified PEP after Prep-", the alternative of 4 intradermal doses (at 4 different sites), on a single visit, at day 0** .
The existing schedule (2x 1 dose IM at day 0 and 3) remains unchanged In the 'simplified PEP after PrEP' situation.
Also the 'PEP schedule, without previous PrEP' was left unchanged.
In regard to the **administration of human rabies immunoglobulines**, the new Belgian guidelines will advise **to inject the maximum (feasible) amount (with a minimal injection of 2 ml) of the calculated dose (20 IU/kg) HRIG, in and around the wound, but the remaining amount should no longer be administered IM at a distant site.** (WHO-SAGE stated that the injection of remaining RIG distant to the wound would be unlikely to confer additional protection). Only in specific situations where the act of injecting the HRIG is technically not possible, the HRIG can be given intramuscular (ipsilateral of the wound).
Ten days after completion of PEP the 'rapid fluorescent focus inhibition test' RFFIT can performed to evaluate the efficaciousness of the series of vaccines. In the former guidelines RIFFT was performed in Schema 2 (at day 31), and in Schema 3 (at day 38); In the new guidelines it is advised to only perform the RIFFT for Schema 3 (no longer for schema 2,

exept in the specific situation of immunosuppressed, or chronically ill patients, or if the vaccines were started abroad).

Monkey bites are frequently seen in tourists, most often when travelling in (South-East) Asia, but these monkey are exceptionally infected with rabies. Therefore, in the new guidelines, even *for monkey injuries of category 3, HRIG are no longer recommended*. More attention should be given to the possibility of transmission of **herpes virus B** (macaque species, which are highly prevalent in Asia, also in urbanized setting, are frequently infected), and prophylaxis with acyclovir can be considered.