Belgian consensus meeting
Travel Medicine
24 June 2016

Patrick Soentjens
Ula Maniewski
Yves Van Laethem
Consensus meeting

24 June 2016
13h30
WIV-ISP Nélis

Patrick Soentjens (ITG – BE Defense)
Ula Maniewski (ITG)
Yves Van Laethem, Charlotte Martin (St-Pierre, ULB)
Frédérique Jacobs, Maya Hites (Erasme, ULB)
Willy Peetermans (KUL Leuven)
Steven Callens (UZ Gent)
Bernard Vandercam (St-Luc, UCL)
Patrick Lacor, Rembert Mertens (UZ Brussel, VUB)
Philippe Léonard (CHU, Ulg)
Sophie Quolin (WIV-ISP)
Jeroen Vanderhilst (Jessa)
Consensus meeting

• No consensus text (Dutch – French) anymore!
• English summary of the consensus meeting 2016 by Patrick Lacor will be published online
• Powerpoint will be online available soon after this meeting
The consensus meeting was chaired by Patrick Soentjens
Secretary of the meeting was Patrick Lacor
The preliminary powerpoint presentations were prepared by Ula Maniewski
and Patrick Soentjens and were presented by both and Yves Van Laethem

The discussion and recommendations of the meeting are
included in the final presentation (published on www.itg.be)

These documents will serve as a proposal for approval by the
governmental Belgian Health Council - section vaccinations, on
15 September 2016

Responsible for final redaction: Patrick Soentjens
Consensus meeting
Program

• Yellow fever: are there any changes? (25’)
• Travelers diarrhea: new guidelines (30’)
• Zika update (10’)
• The pregnant traveller (10’)
• Malaria overview (15’)
• Other topics (20’)
Program

• Yellow Fever
• Travelers diarrhea
• Zika
• The pregnant traveller
• Malaria
• Other topics
• Amendment to International Health Regulations (2005), Annex 7 (yellow fever):

“as of 11 July 2016, for both existing or new certificates, revaccination or a booster dose of yellow fever vaccine cannot be required of international travellers as a condition of entry into a State Party, regardless of the date their international certificate of vaccination was initially issued.”
• No new certificate is needed
• “Countries and health care providers continue to be free to make requirements on vaccination, revaccination or boosters for their own populations, or patients, respectively.”

➔ No WHO guidelines about
  – suboptimal protection in certain subpopulations
  – booster injections

➔ each country creates its own guidelines
### Countries with risk of yellow fever transmission and countries requiring yellow fever vaccination

<table>
<thead>
<tr>
<th>Country</th>
<th>Country with risk of yellow fever transmission</th>
<th>Country requiring yellow fever vaccination for travellers arriving from</th>
<th>Country statement on period of validity for yellow fever vaccination certificate</th>
</tr>
</thead>
<tbody>
<tr>
<td>Afghanistan</td>
<td>Yes</td>
<td>all countries</td>
<td>Not communicated</td>
</tr>
<tr>
<td>Albania</td>
<td>Yes (≥ 1 year)</td>
<td>all countries</td>
<td>Not communicated</td>
</tr>
<tr>
<td>Algeria</td>
<td>Yes (≥ 1 year)</td>
<td>Life</td>
<td></td>
</tr>
<tr>
<td>Angola</td>
<td>Yes</td>
<td>Yes (≥ 9 months)</td>
<td>Life</td>
</tr>
</tbody>
</table>

1. Countries with risk of yellow fever transmission
2. Countries requiring yellow fever vaccination
3. Country statement on period of validity for yellow fever vaccination certificate

[http://www.who.int/ith/2016-ith-annex1.pdf?ua=1](http://www.who.int/ith/2016-ith-annex1.pdf?ua=1)
**Yellow Fever Vaccination Recommendations in the Americas, 2013 (15-7-2014)**

- **Low risk area, but yellow fever vaccination is recommended by the Belgian scientific study group on travel medicine, unless there is a contra-indication for vaccination**
- **Strongly recommended or even obligatory**
- **Vaccination not recommended**

For Details See [WWW.ITG.BE](http://WWW.ITG.BE)
Belgian YF guidelines

• Lifelong protection after 1 YF vaccine for every one with normal immunity

• Administration:
  – Validity: from... until “lifelong”

• Doubts about duration of protection exist in special conditions/immunesuppression (cfr next slide)
  → boosters/ testing neutralising Ab can be necessary→
**INTERNATIONAL CERTIFICATE* OF VACCINATION OR PROPHYLAXIS**

This is to certify that [name] ..........................................................

date of birth .................................. sex ........................................
nationality ..............................................................
national identification document, if applicable ................................
whose signature follows ..........................................................

has on the date indicated been vaccinated or received prophylaxis against: (name of disease or condition)

..............................................................

in accordance with the International Health Regulations.

<table>
<thead>
<tr>
<th>Vaccine or prophylaxis</th>
<th>Date</th>
<th>Signature and professional status of supervising clinician</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.</td>
<td>14 JUNI 2016</td>
<td>Dr. C. Staszewski</td>
</tr>
<tr>
<td>2.</td>
<td></td>
<td></td>
</tr>
<tr>
<td>3.</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*Requirements for validity of certificate on page 2.*

**CERTIFICAT* INTERNATIONAL DE VACCINATION OU DE PROPHYLAXIE**

Nous certifions que [nom] ..........................................................
né(e) le ................. de sexe ........................................
et de nationalité ..........................................................
document d'identification national, le cas échéant ..................
dont la signature suit ..........................................................

a été vacciné(e) ou a reçu des agents prophylactiques à la date indiquée contre: (nom de la maladie ou de l'affection)

..............................................................

conformément au Règlement sanitaire international.

<table>
<thead>
<tr>
<th>Manufacturer and batch no. of vaccine or prophylaxis</th>
<th>Certificate valid from</th>
<th>Certificate valid until</th>
<th>Official stamp of the administering centre</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fabricant du vaccin ou de l'agent prophylactique et numéro du lot</td>
<td>24/6/2016</td>
<td>jusqu'au :</td>
<td>Cachet officiel du centre habilité</td>
</tr>
</tbody>
</table>

*Voir les conditions de validité à la page 3.*
Belgium YF guidelines:

Who is not considered lifelong protected after 1 YF vaccination?

1) **Booster before next travel, once**
   - **People with “special condition”:**
     - Children younger than 9 months
     - Pregnant women
     - Interval < 28 days after vaccination with other life attenuated vaccine
   
   **Certificate:** valid until first day of validity + 1 year

2) **Test neutralising antibodies and boost if necessary (or boost after 10 years)**
   - **Immunosuppression:**
     - HIV-infection (any CD4 count)
     - People under immunosuppression (eg reumatologic / auto-immune disease)
   - **High risk situation**
     - Persons working in lab where wild YF is handled in routine
     - Persons working in region with YF outbreak

3) **Booster is usually needed at least once; or test neutralising Ab before travel**
   - Persons who received **stem cell transplantation** after YF vaccine (CAVE exclusion criteria)
INTERNATIONAL CERTIFICATE* OF VACCINATION OR PROPHYLAXIS

This is to certify that [name] .................................................................
date of birth ................................ sex ..............................................
nationality ........................................................ national identification document, if applicable ..............................................
whose signature follows .................................................................
has on the date indicated been vaccinated or received prophylaxis against (name of disease or condition) .................................................................
in accordance with the International Health Regulations.

<table>
<thead>
<tr>
<th>Vaccine or prophylaxis</th>
<th>Date</th>
<th>Signature and professional status of supervising clinician</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>14 JUNI 2016</td>
<td>Dr. U. Manelewski 1/954/156/580 Patiententcavatie 43/3</td>
</tr>
</tbody>
</table>

* Requirements for validity of certificate on page 2.

CERTIFICAT* INTERNATIONAL DE VACCINATION OU DE PROPHYLAXIE

Nous certifions que [nom] .................................................................
né(e) le ................................ de sexe ..............................................
et de nationalité ........................................................ document d'identification national, le cas échéant ..............................................
dont la signature suit .................................................................
a été vacciné(e) ou a reçu des agents prophylactiques à la date indiquée contre; (nom de la maladie ou de l'affection) .................................................................
conformément au Règlement sanitaire international.

<table>
<thead>
<tr>
<th>Manufacturer and batch no. of vaccine or prophylaxis</th>
<th>Certificate valid from:</th>
<th>Certificate valid until:</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fabricant du vaccin ou de l'agent prophylactique et numéro du lot</td>
<td>24/6/2016</td>
<td>24/6/2017</td>
</tr>
</tbody>
</table>

* Voir les conditions de validité à la page 3.
Example 1

- Pregnant mother vaccinated against yellow fever the 14th of June 2016 for a travel to Uganda
- Validity: from 24 of June 2016 until the 24 of June 2017
- Revaccinate before next travel or after one year
INTERNATIONAL CERTIFICATE* OF VACCINATION OR PROPHYLAXIS

This is to certify that [name] ..........................................................
date of birth ................................... sex ....................................
nationality .................................................................
national identification document, if applicable ................................
whose signature follows ...........................................................
has on the date indicated been vaccinated or received prophylaxis against: (name of disease or condition)

in accordance with the International Health Regulations.

<table>
<thead>
<tr>
<th>Vaccine or prophylaxis</th>
<th>Date</th>
<th>Signature and professional status of supervising clinician</th>
<th>Manufacturer and batch no. of vaccine or prophylaxis</th>
<th>Certificate valid from: until:</th>
</tr>
</thead>
<tbody>
<tr>
<td>FEVER JAUNE</td>
<td>1.7 DECEMBER 2015</td>
<td>Signature et titre du clinicien responsable</td>
<td>Fabricant du vaccin ou de l'agent prophylactique et numéro de lot</td>
<td>27/12/2017 jusqu'au 27/12/2025</td>
</tr>
</tbody>
</table>

* Requirements for validity of certificate on page 2.

CERTIFICAT* INTERNATIONAL DE VACCINATION OU DE PROPHYLAXIE

Nous certifions que [nom] ...................................................
né(e) le ................................... de sexe ................................
et de nationalité ............................................................
document d'identification national, le cas échéant ................................
dont la signature suit ..........................................................
a été vacciné(e) ou a reçu des agents prophylactiques à la date indiquée contre: (nom de la maladie ou de l'affection)

conformément au Règlement sanitaire international.

* Voir les conditions de validité à la page 3.
Example 2

- HIV patient under ART with CD4 above 500 was vaccinated against yellow fever the 17th of December 2016 for a travel to Angola.
- Validity: from 27 of December 2015 until 27 of December 2025.
- Retest by neutralizing antibodies via ITM Antwerp.
- Revaccinate after ten years.
Yellow fever Neutralizing antibodies

- Send one serum tube to the National Reference Centre for flaviviridae, ITM Antwerp
- Results will be available after three weeks
- The test is for free, when criterium of immunosuppression is full-filled
- Please always note immunosuppression on the request form
- Ideal timing for testing after booster vaccination is 28 days

Link labo guide ITG

Link website NRC's
Certificate / Carnet

• You can order the certificates by mail: via bookorders@who.int

• Address:
WHO PRESS / EDITIONS OMS / EDICIONES DE LA OMS
CH-1211 GENEVA 27
SWITZERLAND
WHO Press: Direct Tel. +41 22 791.32.64
Direct Fax +41 22 791.48.57

• Web: www.who.int/bookorders

Ordering via Dr Wagner Saniport Belgium not possible anymore end 2017!
Figure 1. Monthly time line of infected districts in Angola, December 2015 to 1 June 2016
Figure 3. Distribution of yellow fever confirmed cases in Angola and Democratic Republic of the Congo as of 15 June 2016.
Figure 3. National weekly number of suspected and confirmed yellow fever cases in Angola, 5 December 2015 to 3 June 2016

Data provided by Angola yellow fever situation report as of 6 June 2016.
Ghana reports yellow fever in Brong-Ahafo and Volta regions
According to a press statement by the Ghana Health Services published in local media, over the past four weeks, health officials have received reports of confirmed Yellow Fever (YF) cases from the Brong-Ahafo and Volta regions. A total of four cases...

Ethiopia: 22 suspected yellow fever cases being investigated
Ethiopia is one of three African countries reporting suspected yellow fever cases potentially linked to the Angola outbreak. According to UN health officials, the suspect cases are reported from Republic of Congo (one case), Sao Tome and Principe (two...

Yellow fever: DRC imported cases from Angola
As of 31 May, a total of 700 suspected yellow fever (YF) cases, including 63 deaths, had been reported from all the provinces in the Democratic Republic of Congo (DRC) by the national surveillance system. To date, a total of 52 cases have been laboratory-confirmed...
INVASIVE MOSQUITO - NETHERLANDS (NOORD HOLLAND)

A ProMED-mail post
<http://www.promedmail.org>
ProMED-mail is a program of the
International Society for Infectious Diseases <http://www.isid.org>

Date: Wed 22 Jun 2016
Source: Dutch News [edited]

The product safety board NVWA is to step up its monitoring of mosquitoes at Amsterdam's Schiphol airport following the discovery of 3 yellow fever mosquitoes in 2 separate traps. The mosquitoes can spread diseases such as dengue, West Nile fever, and yellow fever, but the 3 at Schiphol were unlikely to be carriers, the NWVA said. In addition, the new find poses no risks to the public because the mosquitoes were not found in passenger areas, according to the public health institute RIVM.
WHO Strategic Advisory Group of Experts (SAGE) “using a fifth of a standard vaccine dose would still provide protection against the disease for at least 12 months and possibly much longer.

A yellow fever vaccine given at a fractional dose would not qualify for a yellow fever certificate under the IHR requirements. Travellers will need to obtain the full dose of the vaccine to be eligible for the yellow fever certificate.
Reminder: side effects

- **Anaphylaxis** (eggs/gelatine)
  - 1.8/100 000 doses

- **YEL-AND**: conglomerate of clinical syndroms (meningoenceph., GBS, ADEM, cranial n. palsy, ...)
  - 3-28 days post-vaccine
  - Historically infants, now cases reports all ages

- **YEL-AVD**: similar to wild disease
  - 0-8 days post-vaccine
  - >65 cases reported since 2001

- **Primary vaccination**
  - Rarely fatal
  - 0.8/100 000 doses
  - 60-69 y: 1.6/100 000 doses
  - ≥70 y: 2.3/100 000 doses

- **Primary vaccination**
  - 60% CFR
  - 0.4/100 000 doses
  - 60-69 y: 1/100 000 doses
  - ≥70 y: 2.3/100 000 doses
In case of suspicion of YEL AVD or YEL AND: special procedure

Please inform us as well
### TABLE 2. Contraindications and precautions to yellow fever vaccine administration

#### Contraindications

- Allergy to vaccine component
- Age less than 6 months
- Symptomatic HIV infection or CD4+ T-lymphocytes <200/mm³ (or <15% of total in children aged <6 years)*
- Thymus disorder associated with abnormal immune function†
- Primary immunodeficiencies
- Malignant neoplasms
- Transplantation
- Immunosuppressive and immunomodulatory therapies†

#### Precautions

- Age 6–8 months
- Age ≥60 years†
- Asymptomatic HIV infection and CD4+ T-lymphocytes 200–499/mm³ (or 15%–24% of total in children aged <6 years)*
- **Pregnancy**
- **Breastfeeding**

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2012 Relapsing remitting MS
Quid immunosuppression?

A réviser
Vaccination recommendations for adult patients with autoimmune inflammatory rheumatic diseases

Silja Bähler, Gilles Eperon, Camillo Ribi, Diego Kyburz, Fons van Gompel, Leo G. Visser, Claire-Anne Siegrist, Christoph Hatz

The Immunosuppressed Traveler

L.G. Visser, MD, PhD*

KEYWORDS
- Immuno compromised
- Immunosuppressive agents
- Travel health information
- Vaccines
- Tumor necrosis factor antagonist
- Immune reconstitution
- Hematopoietic cell transplantation
- HIV
Vaccinatie is pas mogelijk vanaf **3 maanden** na het stoppen van immuundemprimerende medicatie en chemotherapie.

Uitzonderingen op deze regel: minimale wachttijd na het stoppen

<table>
<thead>
<tr>
<th>Generisch produkt</th>
<th>Product</th>
<th>Wacht</th>
</tr>
</thead>
<tbody>
<tr>
<td>Prednison ≥ 20 mg per dag</td>
<td></td>
<td>1 maand</td>
</tr>
<tr>
<td>Azathioprine</td>
<td>Imuran</td>
<td>2 maanden</td>
</tr>
<tr>
<td>Cyclosporine</td>
<td>Neoral/Sandimmun</td>
<td>1 week</td>
</tr>
<tr>
<td>Etanercept</td>
<td>Enbrel</td>
<td>1 maand</td>
</tr>
<tr>
<td>Everolimus</td>
<td>Certican</td>
<td>9 dagen</td>
</tr>
<tr>
<td>Methotrexat</td>
<td>Ledertrexate</td>
<td>1-3 maanden</td>
</tr>
<tr>
<td>Mycophenolate</td>
<td>Cellcept</td>
<td>1 week</td>
</tr>
<tr>
<td>Rituximab</td>
<td>Mabthera</td>
<td>&gt; 12 maanden</td>
</tr>
<tr>
<td>Tacrolimus</td>
<td>Prograf</td>
<td>3 dagen</td>
</tr>
<tr>
<td>Alemtuzumab</td>
<td>Lemtrada</td>
<td>&gt; 12 maanden</td>
</tr>
<tr>
<td>Leflunomide</td>
<td>Arava</td>
<td>&gt; 2 jaar</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Tenzij wash out met cholestyramine</td>
</tr>
</tbody>
</table>
La vaccination est possible 3 mois après l'arrêt d'une médication immunosuppressive ou d'une chimiothérapie. Il y des exceptions à cette règle. Période à laisser passer après l’arrêt d’un traitement :

<table>
<thead>
<tr>
<th>Produit génétique</th>
<th>Produit</th>
<th>Attendez</th>
</tr>
</thead>
<tbody>
<tr>
<td>Prednison ≥ 20 mg par jour</td>
<td></td>
<td>1 mois</td>
</tr>
<tr>
<td>Azathioprine</td>
<td>Imuran</td>
<td>2 mois</td>
</tr>
<tr>
<td>Cyclosporine</td>
<td>Néoral/Sandimmun</td>
<td>1 semaine</td>
</tr>
<tr>
<td>Etanercept</td>
<td>Enbrel</td>
<td>1 mois</td>
</tr>
<tr>
<td>Everolimus</td>
<td>Certican</td>
<td>9 jours</td>
</tr>
<tr>
<td>Méthotrexaat</td>
<td>Ledertrexate</td>
<td>1-3 mois</td>
</tr>
<tr>
<td>Mycophénolate</td>
<td>Cellcept</td>
<td>1 semaine</td>
</tr>
<tr>
<td>Rituximab</td>
<td>Mabthera</td>
<td>&gt; 12 mois</td>
</tr>
<tr>
<td>Tacrolimus</td>
<td>Prograft</td>
<td>3 jours</td>
</tr>
<tr>
<td>Alemtuzumab</td>
<td>Lemtrada</td>
<td>&gt; 12 mois</td>
</tr>
<tr>
<td>Leflunomide</td>
<td>Arava</td>
<td>&gt; 2 ans (excepté en cas de washout par choléstyramine)</td>
</tr>
</tbody>
</table>
Guide des vaccinations des patients atteints de maladies rhumatismales sous traitement immunosuppresseur

Very visual information about general rules of vaccinations in immunosuppression
Reminder: other mandatory vaccines

- Yellow fever
- Meningococcal disease
- Polio

Ensure enough capacity in your Travel clinic during spring and summer!
Where to find information?

Always use the most recent electronic edition
Never use old outdated editions!

Since 2008-2009 only electronic version:

www.itg.be

http://wwwn.cdc.gov/travel/contentYellowBook.aspx

www.who.int/ith
Program

• Yellow Fever
• Travelers diarrhea
• Zika
• The pregnant traveller
• Malaria
• Other topics
Selftreatment Travelers’ Diarrhea in Belgian travellers?

Belgium does not follow the recommendations to treat TD with antibiotics as liberally as the US does, but the treatment policy is not as restrictive as in Scandinavia and in the Netherlands.

The present Belgian recommendations have been drawn up years ago by infectiologists after intense discussions. The recent publication of Kantele et al. has however forced us to rethink in 2016 the recommendations, and asks for a balanced discussion, taking into account the following:

- What is the impact of a one-day antibiotic treatment, the schedule most often advised for (uncomplicated) diarrhea,
- In which circumstances? To prevent ruining the trip?
- Clinical evidence suggests that the Belgian traveler sparsely takes antibiotic treatment rather than overusing it.
- Restricting antibiotic self-treatment may increase (avoidable) hospitalization in low income country setting (& wrong antibiotic use)
- Reviewing the TD treatment policy would preferentially be based on prospective study data, that are not yet available.....
Travelers diarrhea

Review

Traveler’s Diarrhea
A Clinical Review

Robert Steffen, MD; David R. Hill, MD, DTM&H; Herbert L. DuPont, MD

Figure. Incidence Rates of Traveler’s Diarrhea in the Initial 2 Weeks of Stay in Various Regions of the World Among Visitors Residing in Industrialized Countries, 1996-2008

JAMA 2015
Travelers diarrhea

New Developments in Traveler’s Diarrhea

Javier de la Cabada Bauche, MD, and Herbert L. DuPont, MD

Gastroenterology – Hepatology 2011
Travelers diarrhea

- Travelers diarrhea as a disease
- Perspective of the traveler
- Carriage of MDR germs
Travelers diarrhea

Risk between 8-20 % for a two week trip
Sometimes a heavy disease in 15-20 %
Estimated 17 million patients yearly with TD
Some seek medical advice (38%) > suffering
Some need to change their travel plans > loss of leisure - loss of money

Sequelae:
Postinfection IBS (3-20%)
Reactive arthritis (2-52%)
Guillain Barré (1/1000)

Antibiotics for TD

CONs

INDIVIDUAL
- Self-limiting
- Increased risk of ESBL and CPE carriage
- Possible SAE of antibiotics
- Possible QTc prolongation
- Change in microbiome

POPULATION
- Selecting for multiresistant strains
- Reduction of efficacy of antibiotic in the future
- More MDR related infections and hospital costs

Reduced use of antibiotics
Reduced selection of MDR strains
Improved AB stewardship
Lesser MDR related infections
Lesser hospital costs

Behrens NECTM2016
Antibiotics for TD
PROs

INDIVIDUAL

• Shorten disease with 1 to 1.5 days in 30-70% of cases from 3 to 1.5 days
• Prevent loss of leisure time
• Cost saving
• Reduced complications
• Prevents inappropriate hospitalizations abroad

Behrens NECTM2016

Travelers diarrhea

<table>
<thead>
<tr>
<th>Public</th>
<th>Personal</th>
</tr>
</thead>
<tbody>
<tr>
<td>Reduced use of antibiotics</td>
<td>Shorter illness</td>
</tr>
<tr>
<td>Reduced selection of ESBL etc.</td>
<td>Prevent loss of leisure time</td>
</tr>
<tr>
<td>Improved antibiotic stewardship</td>
<td>Cost saving</td>
</tr>
<tr>
<td>Evidence of ESBL causally associated with morbidity</td>
<td>Reduced complications</td>
</tr>
<tr>
<td>Travel associated carriage a threat to the communities health</td>
<td>Carriage a threat to the individual’s health</td>
</tr>
</tbody>
</table>

ESBL > Public Health morbidity?  
MDR Carriage > Public Health issues?  

Is carriage a threat for the individual?

Behrens NECTM2016
Travelers diarrhea

Our responsibility?

**Summary**

- TD has an important economic and social (morbidity) cost to travellers
- Antibiotics reduce morbidity and are a preferred Rx
- Antibiotics increase the carriage of MRE
- A health consequence of carriage (pop. & pers.) has not been shown
- A global and multi sector strategy to reduce selection of MRE is necessary.

Behrens NECTM2016
Travelers' diarrhea

N = 486
EU > D
US - CAN

Travelers' Preferences for Diarrheal Treatments and Prophylaxis

North American travelers (n=277)
European travelers (n=209)

p < 0.001

p < 0.001

p < 0.001

Antibiotic A
Antibiotic B
No treatment

FQ
RIF

Ericsson et al JTM 2009

THE TRAVELERS’ PERSPECTIVE
N= 212
89 (42%) had mild TD and 123 (58%) had **moderate or severe** TD.

**Outcome data**

N= 84

N= 270/1120 24%
US Mil
T < 6.5 m
With AB standby

**Table 3  Outcomes associated with travelers’ diarrhea (TD) self-treatment**

<table>
<thead>
<tr>
<th>Outcome characteristics</th>
<th>Optimal self-treatment (no treatment or anti-diarrheals) (n = 33)</th>
<th>Suboptimal self-treatment (antibiotics + anti-diarrheals) (n = 7)</th>
<th>p-Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>TLUS, median h (IQR)†</td>
<td>8.5 (3.5–25.0)</td>
<td>14.0 (7.3–27.3)</td>
<td>0.22</td>
</tr>
<tr>
<td>Clinical cure at 24 hours, n (%)</td>
<td>23 (70)</td>
<td>4 (57)</td>
<td>0.66</td>
</tr>
<tr>
<td>Clinical cure at 48 hours, n (%)</td>
<td>28 (85)</td>
<td>7 (100)</td>
<td>0.36</td>
</tr>
<tr>
<td>Post-treatment side effects</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Nausea, n (%)</td>
<td>0 (0)‡</td>
<td>1 (14)</td>
<td>0.35</td>
</tr>
<tr>
<td>Vomiting, n (%)</td>
<td>1 (8)‡</td>
<td>0 (0)</td>
<td>1.0</td>
</tr>
</tbody>
</table>

**Moderate or severe diarrhea (n = 84)**

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Optimal self-treatment (antibiotics + anti-diarrheals) (n = 37)</th>
<th>Suboptimal self-treatment (no treatment or anti-diarrheals) (n = 47)</th>
<th>p-Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>TLUS, median h (IQR)†</td>
<td>7 (2–62)</td>
<td>8.5 (2.5–38.5)</td>
<td>0.97</td>
</tr>
<tr>
<td>Clinical cure at 24 hours, n (%)</td>
<td>24 (65)</td>
<td>30 (64)</td>
<td>0.92</td>
</tr>
<tr>
<td>Clinical cure at 48 hours, n (%)</td>
<td>27 (73)</td>
<td>36 (77)</td>
<td>0.70</td>
</tr>
<tr>
<td>Post-treatment side effects</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Nausea, n (%)</td>
<td>11 (30)§</td>
<td>0 (0)§</td>
<td>0.005</td>
</tr>
<tr>
<td>Vomiting, n (%)</td>
<td>5 (14)§</td>
<td>0 (0)§</td>
<td>0.15</td>
</tr>
</tbody>
</table>

TLUS, time to last unformed stool; IQR, interquartile range.

**Moderate or severe TD** was independently associated with sub-optimal self-treatment (OR 10.4)

Are our travelers enough informed how to use AB?

**The Travelers’ Perspective**

Lalani et al JTM 2015
Inconvenience due to travelers’ diarrhea: a prospective follow-up study

Darius Soonawala*, Jessica A Vlot and Leo G Visser

Table 2 Travelers’ diarrhea, incidence proportions and incidence rates for 390 Dutch travelers.

<table>
<thead>
<tr>
<th>Travel destination</th>
<th>Travelers -</th>
<th>TD cases -</th>
<th>TD incidence proportion - %</th>
<th>Mean travel duration - days</th>
<th>TD Incidence rate - per 100 pdt (SE)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>( n )</td>
<td>( n )</td>
<td>(SE)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Northern Africa</td>
<td>17</td>
<td>7</td>
<td>41 (12.3)</td>
<td>10.4</td>
<td>3.95 (1.47)</td>
</tr>
<tr>
<td>South-central Asia</td>
<td>31</td>
<td>16</td>
<td>52 (9.1)</td>
<td>20.2</td>
<td>2.55 (0.63)</td>
</tr>
<tr>
<td>Central America and Caribbean</td>
<td>24</td>
<td>11</td>
<td>46 (10.4)</td>
<td>18.9</td>
<td>2.42 (0.72)</td>
</tr>
<tr>
<td>South-eastern Asia</td>
<td>121</td>
<td>61</td>
<td>50 (4.6)</td>
<td>22.5</td>
<td>2.25 (0.28)</td>
</tr>
<tr>
<td>Eastern Africa</td>
<td>57</td>
<td>25</td>
<td>44 (6.6)</td>
<td>23.4</td>
<td>1.88 (0.37)</td>
</tr>
<tr>
<td>Central Africa</td>
<td>7</td>
<td>3</td>
<td>43 (20.2)</td>
<td>23.4</td>
<td>1.83 (1.05)</td>
</tr>
<tr>
<td>Central and Western Asia</td>
<td>32</td>
<td>8</td>
<td>25 (7.8)</td>
<td>14.3</td>
<td>1.75 (0.61)</td>
</tr>
<tr>
<td>Western Africa</td>
<td>15</td>
<td>7</td>
<td>47 (13.3)</td>
<td>28.6</td>
<td>1.63 (0.61)</td>
</tr>
<tr>
<td>Southern Africa</td>
<td>15</td>
<td>4</td>
<td>27 (11.8)</td>
<td>23.1</td>
<td>1.16 (0.58)</td>
</tr>
<tr>
<td>Eastern Asia</td>
<td>36</td>
<td>11</td>
<td>31 (7.8)</td>
<td>29.4</td>
<td>1.04 (0.31)</td>
</tr>
<tr>
<td>South America</td>
<td>46</td>
<td>7</td>
<td>15 (5.4)</td>
<td>26.4</td>
<td>0.58 (0.22)</td>
</tr>
<tr>
<td><strong>All travelers</strong></td>
<td><strong>401¹</strong></td>
<td><strong>160</strong></td>
<td><strong>41 (2.4)†</strong></td>
<td><strong>22.4</strong></td>
<td><strong>1.78 (0.14)</strong></td>
</tr>
</tbody>
</table>

N= 160
Dutch
T < 3 m
Without AB

THE TRAVELERS’ PERSPECTIVE
### THE TRAVELERS’ PERSPECTIVE

N= 160/401 (39%) Dutch T < 3 m Without AB

<table>
<thead>
<tr>
<th>Destination</th>
<th>N = 160 cases TD incidence proportion</th>
</tr>
</thead>
<tbody>
<tr>
<td>Asia</td>
<td>96/220 43.5%</td>
</tr>
<tr>
<td>Africa</td>
<td>46/111 41.5%</td>
</tr>
<tr>
<td>Central and South America</td>
<td>18/70 25.5%</td>
</tr>
</tbody>
</table>
INCONVENIENCE

Objective criteria
A. Stool frequency
   Watery stool duration
   Fecal urge duration
   Abdominal cramps
   Nausea
   Vomiting
   Fever
B. No changes in program
   Altered the program
   Confined to the accommodation

Subjective criteria
No > Minor > Moderate > Large > Severe

THE TRAVELERS’ PERSPECTIVE
Table 3 Characteristics of the episode of travelers’ diarrhea for 160 Dutch travelers, stratified by the objective degree of inconvenience.

<table>
<thead>
<tr>
<th>Objective degree of inconvenience - n (%)</th>
<th>Conducted program as planned</th>
<th>Forced to alter program</th>
<th>Confined to accommodation</th>
<th>Total 160</th>
</tr>
</thead>
<tbody>
<tr>
<td>107/160 (67%)</td>
<td>33/160 (21%)</td>
<td>20/160 (13%)</td>
<td></td>
<td>160 (100%)</td>
</tr>
</tbody>
</table>

(Continued)

<table>
<thead>
<tr>
<th>Vomiting - n (%)*</th>
<th>Conducted program as planned</th>
<th>Forced to alter program</th>
<th>Confined to accommodation</th>
<th>Total 160</th>
</tr>
</thead>
<tbody>
<tr>
<td>12 (36)</td>
<td>8 (7)</td>
<td>11 (55)</td>
<td></td>
<td>17 (11)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Treatment - n (%)</th>
<th>Conducted program as planned</th>
<th>Forced to alter program</th>
<th>Confined to accommodation</th>
<th>Total 160</th>
</tr>
</thead>
<tbody>
<tr>
<td>Loperamide</td>
<td>29 (27)</td>
<td>11 (33)</td>
<td>14 (70)</td>
<td>54 (34)</td>
</tr>
<tr>
<td>Activated carbon</td>
<td>3 (3)</td>
<td>6 (18)</td>
<td>2 (10)</td>
<td>11 (7)</td>
</tr>
<tr>
<td>Antimicrobial agent</td>
<td>3 (3)</td>
<td>6 (18)</td>
<td>5 (25)</td>
<td>14 (9)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Subjective degree of inconvenience - n (%)</th>
<th>Conducted program as planned</th>
<th>Forced to alter program</th>
<th>Confined to accommodation</th>
<th>Total 160</th>
</tr>
</thead>
<tbody>
<tr>
<td>None/Minor</td>
<td>58 (54)</td>
<td>5 (15)</td>
<td>-</td>
<td>63 (39)</td>
</tr>
<tr>
<td>Moderate</td>
<td>33 (31)</td>
<td>13 (39)</td>
<td>8 (40)</td>
<td>54 (34)</td>
</tr>
<tr>
<td>Large/Severe</td>
<td>16 (15)</td>
<td>15 (46)</td>
<td>12 (60)</td>
<td>43 (27)</td>
</tr>
</tbody>
</table>
‘If you were contracting severe TD, how large a problem would you consider this to be?’

Table 5 How did an episode of travelers’ diarrhea (TD) influence travelers’ perception of TD? The expected amount of subjective inconvenience due to travelers’ diarrhea before and after travel is stratified by whether travelers had TD.*

<table>
<thead>
<tr>
<th></th>
<th>Travelers who had TD n = 160</th>
<th>Travelers who did not have TD n = 230</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Before departure</td>
<td>After returning</td>
</tr>
<tr>
<td>No problem - n (%)</td>
<td>1 (1)</td>
<td>11 (7)</td>
</tr>
<tr>
<td>A small problem - n (%)</td>
<td>22 (14)</td>
<td>42 (26)</td>
</tr>
<tr>
<td>Neither a small nor a large problem - n (%)</td>
<td>51 (32)</td>
<td>56 (35)</td>
</tr>
<tr>
<td>A large problem - n (%)</td>
<td>69 (43)</td>
<td>49 (31)</td>
</tr>
<tr>
<td>A very large problem - n (%)</td>
<td>17 (11)</td>
<td>2 (1)</td>
</tr>
</tbody>
</table>

Those who experienced TD would estimate the impact lower in retrospect
Travelers diarrhea

Prospective study in TD with severe diarrhea or inconvenience??
(objective – subjective definitions)

Randomization

> Questionnaire

> Real-life identification of causal agent during TD

With antibiotic

Effect on inconvenience

Without antibiotic
Travelers diarrhea

Prospective study in TD with questionnaire in Belgium

Preliminary data

N = > 600 included
269 returned their questionnaire
1/3 with TD
25 % used antibiotics

PI Jeroen Vanderhilst
Jessa
Travelers diarrhea and ESBL carriage

FIG 1 ESBL carriage rates in the community, according to their geographical and temporal distribution. Each bubble area is proportional to the size of the corresponding study. The lines represent the evolution of ESBL-E carriage.
Travelers diarrhea

From colonisation to infection...

Asia travel is a risk factor for CA-ESBL+
UTI: OR 21 (4.5-97)

Soraas, Plos One 2013

Travel is a risk factor for severe sepsis after prostatic
Bx: RR 2.7 (1.0-7.1)

Patel, BJU, 2011
Travelers diarrhea

Clinical Infectious Diseases Advance Access published January 21, 2015

Antimicrobials Increase Travelers’ Risk of Colonization by Extended-Spectrum Betalactamase-Producing Enterobacteriaceae

Anu Kantele,1,2,3,4 Timja Lääveri,1,2 Sointu Mero,5 Katri Vilkman,2,3 Sari H. Pakkanen,3 Jukka Ollgren,6 Jenni Antikainen,5 and Juha Kirveskari5

1Department of Clinical Medicine, University of Helsinki, 2Division of Infectious Diseases, Department of Medicine, Helsinki University Hospital, and 3Department of Bacteriology and Immunology, University of Helsinki, 4Aava Travel Clinic, Medical Centre Aava, 5Department of Clinical Microbiology, Helsinki University Hospital, University of Helsinki, and 6National Institute for Health and Welfare, Helsinki, Finland
Travelers diarrhea

Background
- More than 300 million travelers visit regions with poor hygiene annually. A significant percentage of them become colonized by resistant intestinal bacteria such as extended-spectrum beta-lactamase-producing Enterobacteriaceae (ESBL-PE) and may transmit the strains to others and to medical care settings when they return home.

Methods
- Stool samples were collected from 430 Finns before and after traveling outside Scandinavia.
- All specimens were analyzed for ESBL- and carabapenemase-producing Enterobacteriaceae (CPE).
- Questionnaires were used to survey volunteers about use of antimicrobials as well as other potential risk factors.

Results
- 21 % (90/430) of the travelers became colonized by ESBL-PE - none by CPE.
- Were identified as independent predisposing risk factors
  1. Geographic region
  2. occurrence of travelers’ diarrhea (TD)
  3. age
  4. use of antimicrobial (AB) for TD
<table>
<thead>
<tr>
<th>Age group (years)</th>
<th>0-17</th>
<th>18-30</th>
<th>31-50</th>
<th>51-64</th>
<th>65+</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male</td>
<td>262 (81)</td>
<td>146 (34)</td>
<td>119 (28)</td>
<td>90 (21)</td>
<td>41 (10)</td>
</tr>
<tr>
<td>Female</td>
<td>34 (8)</td>
<td>2 (2)</td>
<td>32 (9)</td>
<td>7 (8)</td>
<td>34 (10)</td>
</tr>
<tr>
<td>Age (years)</td>
<td>0-17</td>
<td>18-30</td>
<td>31-50</td>
<td>51-64</td>
<td>65+</td>
</tr>
<tr>
<td>Mean</td>
<td>40 (range: 0-77)</td>
<td>41 (range: 0-76)</td>
<td>39 (range: 11-77)</td>
<td>64 (range: 20-84)</td>
<td>79 (range: 17-85)</td>
</tr>
<tr>
<td>SD</td>
<td>17.2</td>
<td>16.1</td>
<td>17.5</td>
<td>N/A</td>
<td>N/A</td>
</tr>
<tr>
<td>Geographic region</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>South Asia</td>
<td>61 (14)</td>
<td>38 (11)</td>
<td>23 (10)</td>
<td>N/A</td>
<td>N/A</td>
</tr>
<tr>
<td>Southeast Asia</td>
<td>101 (24)</td>
<td>33 (9)</td>
<td>69 (21)</td>
<td>N/A</td>
<td>N/A</td>
</tr>
<tr>
<td>East Asia</td>
<td>6 (1)</td>
<td>2 (2)</td>
<td>4 (1)</td>
<td>N/A</td>
<td>N/A</td>
</tr>
<tr>
<td>North Africa and the Middle East</td>
<td>12 (3)</td>
<td>4 (1)</td>
<td>2 (2)</td>
<td>N/A</td>
<td>N/A</td>
</tr>
<tr>
<td>Sub-Saharan Africa</td>
<td>193 (45)</td>
<td>23 (6)</td>
<td>70 (22)</td>
<td>N/A</td>
<td>N/A</td>
</tr>
<tr>
<td>South America, Central America, and the Caribbean</td>
<td>40 (9)</td>
<td>0 (0)</td>
<td>40 (12)</td>
<td>N/A</td>
<td>N/A</td>
</tr>
<tr>
<td>North America, Europe, Australia</td>
<td>17 (4)</td>
<td>0 (0)</td>
<td>17 (5)</td>
<td>N/A</td>
<td>N/A</td>
</tr>
<tr>
<td>Length of journey (days)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean</td>
<td>19 (5)</td>
<td>27 (5)</td>
<td>17.5 (3)</td>
<td>N/A</td>
<td>N/A</td>
</tr>
<tr>
<td>SD</td>
<td>12.2</td>
<td>13.0</td>
<td>13.9</td>
<td>N/A</td>
<td>N/A</td>
</tr>
</tbody>
</table>

Length of journey (information missing for 93)
- 7 d or less: 50 (15)
- 8–15 d: 162 (47)
- 16–30 d: 96 (28)
- Longer than 30 d: 35 (8)

TD: 285 (77)

Use of antimicrobial medications
- None: 365 (89)
- Antimicrobial for TD: 52 (12)
- Antimicrobial for indications other than TD: 14 (3)

Use of alcohol (information missing for 66)
- 0-2 units/day: 262 (72)
- ≥3 units/day: 102 (28)

Meals with locals (information missing for 24)
- Site of meals (≥50% at restaurants vs. mainly at own household): 345 (83)

Site of meals (information missing for 14)
ESBL – AB – loperamide
Travelers diarrhea

Figure. Study protocol for investigating risk for contracting ESBL-producing Enterobacteriaceae among travelers from Finland with TD. LO–AMD–, not treated with medication; LO+AMD–, treated with LO alone; LO–AMD+, treated with AMDs alone; LO+AMD+, treated with a combination of both drugs. AMD, antimicrobial drugs; ESBL, extended-spectrum β-lactamase; LO, loperamide; TD, travelers’ diarrhea.
<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Total, no. (%)</th>
<th>ESBL neg, no. (%)</th>
<th>ESBL pos, no. (%)</th>
<th>Univariate analysis</th>
<th>Multivariable analysis with imputation</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>p value</td>
<td>OR (95% CI)</td>
</tr>
<tr>
<td>Total</td>
<td>288 (100)</td>
<td>213 (74)</td>
<td>75 (26)</td>
<td>NA</td>
<td>NA</td>
</tr>
<tr>
<td>Study groups</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>LO–AMD–</td>
<td>139 (48)</td>
<td>110 (79)</td>
<td>29 (21)</td>
<td>NA</td>
<td>1.0</td>
</tr>
<tr>
<td>LO+AMD–</td>
<td>90 (31)</td>
<td>72 (80)</td>
<td>18 (20)</td>
<td>0.874</td>
<td>0.9 (0.5–1.8)</td>
</tr>
<tr>
<td>LO–AMD+‡</td>
<td>45 (16)</td>
<td>27 (60)</td>
<td>18 (40)</td>
<td>0.012</td>
<td>2.5 (1.2–5.2)</td>
</tr>
<tr>
<td>LO+AMD+</td>
<td>14 (5)</td>
<td>4 (29)</td>
<td>10 (71)</td>
<td>&lt;0.001</td>
<td>9.5 (2.8–32.4)</td>
</tr>
</tbody>
</table>
A call to restrict prescribing antibiotics for travellers’ diarrhea – Travel medicine practitioners can play an active role in preventing the spread of antimicrobial resistance

Re-thinking prevention and treatment of travelers’ diarrhea – Time for a change?
Travelers diarrhea

ESBL-PE – Relevant to Travelers?

21% of travelers colonized by ESBL-PE
Risk highest in South Asia
Having diarrhea increased risk
Getting antibiotic for diarrhea further increased risk


But, only 9% still positive after 6 months


So what?
Maybe avoid presumptive antibiotic treatment?
Travelers diarrhea

Individual

- Risk of infection low <1%
- The risk is higher than 10%
  when

  Longer colonization time:
  5% > 6 months
  2% > 12 months

Severely ill patients (DM)
Hospitalization (ICU)
Traveler's diarrhea

Finland

350,000 travelers to the tropics/year

- 21% - 73500 new ESBL/year
- 2% - 1470 ESBL carriers > 12 months

MDR transmission to household – to hospitals

Increase background prevalence
More outbreaks

Kantele NECTM2016
Travelers' diarrhoea

Global

350 million travelers to the tropics/year

- 21% - 73.5 million new ESBL/year
- 2% - 1.4 million ESBL carriers > 12 months

MDR transmission to household – to hospitals

Increase background prevalence
More outbreaks

Kantele NECTM2016
Travelers diarrhea

Dutch Combat study N = 2001

Carriage
- MDR-E 80% India
- Colistine-R carriage

Risk factors
- cipro use - TD - IBD
- other eating from stalls - orphanage

How long carriage? 3 months
Transmission to households? 12%
Morbidity related to carriage? ?

Meeting Utrecht, 3 June 2016
Travelers diarrhea

The interaction between prior antimicrobial drug exposure and resistance in human Salmonella infections

Maike Koningstein¹, Jacob Simonsen², Morten Helms³ and Kåre Mølbak¹∗

J Antimicrob Chemother 2010; 65: 1819–1825

Antimicrobial Use: A Risk Factor or a Protective Factor for Acquiring Campylobacteriosis?

Maike Koningstein,¹,² Jacob Simonsen,¹ Morten Helms,³ Tine Hald,⁴ and Kåre Mølbak¹

¹Department of Epidemiology, Statens Serum Institut, Copenhagen, Denmark; ²Department of Epidemiology, RIVM, Bilthoven, the Netherlands; ³Department of Infectious Diseases, Copenhagen University Hospital, Hvidovre, Denmark; and ⁴DTU FOOD, Danmarks Tekniske Universitet, Søborg, Denmark

CID 2011:53 (1 October) • Koningstein et al
Travelers diarrhea
FQ and increased risk on subsequent Salmonella infection

Retrospective case control study
N= 22602

Objectives: The use of antimicrobial drugs for food animals selects for resistant non-typhoid Salmonella strains, but human consumption of antimicrobial drugs may also increase the risk of subsequent infection. The aim of this study was to determine the risk of salmonellosis attributable to human consumption of antimicrobial drugs in a case–control study of 22,602 laboratory-confirmed Salmonella infections, diagnosed in Denmark between 1997 and 2005.

Methods: A population registry-based case–control study, using several Danish databases: the National Prescription Database; the National Registry for Enteric Pathogens; the Civil Registry System; and the Integrated Database on Labour Market Research.

Results: Exposure to trimethoprim, sulphonamides, broad-spectrum penicillins, tetracyclines and fluoroquinolones, during the year prior to diagnosis, was associated with an increased risk of non-typhoid Salmonella infection. Overall, the highest risk was associated with the prior use of fluoroquinolones. This risk increased as the time window of exposure approached the infection date. Previous use of fluoroquinolones was associated with an odds ratio (OR) of 4.55 [95% confidence interval (CI): 3.78–5.47] for Salmonella serotypes other than Salmonella Typhimurium or Salmonella Enteritidis, an OR of 2.21 (95% CI: 1.70–2.86) for Salmonella Typhimurium and an OR of 2.07 (95% CI: 1.76–2.42) for Salmonella Enteritidis. In particular for fluoroquinolones, there was an interaction between the pathogen resistance pattern and a history of antibiotic drug use.

Conclusions: The increasing use of antibiotics, particularly fluoroquinolones, is likely to result in increased incidence of foodborne infections with drug-resistant Salmonella.

J Antimicrob Chemother 2010; 65: 1819–1825
Travelers diarrhea
FQ and increased risk on subsequent Salmonella

Figure 1. Cubic spline plots of the OR of being exposed to broad-spectrum penicillins and fluoroquinolones 0–2 years before infection with Salmonella Typhimurium, Salmonella Enteritidis and other Salmonella, 1997–2005 Denmark. The ORs are adjusted for sex, age, county of residence, population density, income and schooling.

J Antimicrob Chemother 2010; 65: 1819–1825
Travelers diarrhea
FQ and increased risk on subsequent Campylobacter infection

Retrospective case control study
N = 31669

Methods. We conducted a registry-based retrospective case-control study on 31,669 laboratory-confirmed cases of campylobacteriosis between 1999 and 2005 in Denmark. Data were obtained from several Danish databases: the National Registry of Enteric Pathogens, the Danish Civil Registration System, the Danish National Prescription Database, and the Integrated Database on Labor Market Research. Odds ratios (OR) for campylobacteriosis were calculated by conditional logistic regression.

Results. The risk of campylobacteriosis was reduced 1 month after exposure to macrolides (OR, 0.72; 95% confidence interval [CI], 0.56–0.92). Macrolide exposure 1 month to 2 years before infection was associated with an increased risk of a Campylobacter diagnosis (OR, 1.5; 95% CI, 1.4–1.6). A history of fluoroquinolone use was also associated with increased risk (OR, 2.5; 95% CI, 1.8–3.5). This risk was higher for resistant isolates than for susceptible ones.

Conclusions. Treatment with macrolides may protect against Campylobacter infection for a limited period of time, possibly due to the antibacterial effects of the drug or its metabolites. Fluoroquinolone treatment confers increased risk, probably due to a combination of competitive and selective effects, similar to what has been observed for nontyphoid Salmonella infection.
Macrolide and decreased risk on subsequent Campylobacter infection

FQ and increased risk on subsequent Campylobacter infection
Travelers diarrhea

Conclusions (1)

- Increasing resistance in all enteropathogens
  - shift towards use of macrolides (and beyond)

- Revise AB use in the era of MDRO
  - total scope of risks versus genuine benefits?

- Understand better role of disrupted microbiome
  - risk factors, impact, duration, recovery

Erika Vlieghe, MD PhD
Institute of Tropical Medicine, Antwerp
Department of Tropical Diseases, University Hospital Antwerp
Travelers diarrhea

Conclusions (2)

- Select TD patients who will benefit most from AB
  - Severe/invasive presentations
  - Vulnerable/at risk travelers

- Adapt AB by region
  - Asia, (Latin America) → azithromycin
  - Africa → fluoroquinolones

- Inform/invoke travelers in risk-benefit of AB use

- Invest more in prevention research
  - Vaccines, non-absorbables, ...

Erika Vlieghe, MD PhD
Institute of Tropical Medicine, Antwerp
Department of Tropical Diseases, University Hospital Antwerp
Self Treatment
Travellers’ Diarrhea

UK expert group May 2016

10 million deceased/year
Travelers Diarrhea Guidelines

Reasons why guidelines internationally differ:

• Availability of products
• Cultural differences in risk perception
• Lack of evidence (or different interpretation of the same evidence)
• Difference in opinion of experts
• Sometimes public opinion differ
• Who pays?
Idem BE guidelines anno 2015

- Treatment of all moderate and severe TD
- With FQ ( > all continents except Asia)
  - Azithro ( > Asia)
US guidelines

Mild Illness (affected individual does not have to alter his or her schedule)
- Drink fluids (soups, soft drinks)
- Consume saltine crackers
- Consider loperamide treatment: 4 mg (2 capsules) and then 2 mg (1 capsule) after each unformed stool is passed, not to exceed 8 mg/day and for no more than 48 hours

Moderate Illness (affected individual has to alter his or her schedule but is not disabled, is passing ≤5 unformed stools, does not have a fever, and is not passing bloody stools)
- Treatment with 1 of 3 antibiotics:
  - Ciprofloxacin 750 mg (or levofloxacin 500 mg) once a day; may be repeated on Days 2 and 3 if needed
  - Rifaximin 200 mg 3 times per day for 3 days
  - Azithromycin 1,000 mg in a single dose
- Loperamide may be given in a 4-mg single dose with any of these drug treatments for faster initial response.

Severe Illness (affected individual is disabled, has a fever or is passing bloody stools, or is passing ≥6 unformed stools per day)
- Individual has a fever ≥101°F or is passing grossly bloody stools
  - No
  - Yes
    - A single dose of azithromycin 1,000 mg should be taken (though it may cause short-lasting nausea)

De la Cabada Gastroenterology and Hepatology 2011
# Table 3 | Summary of self treatment choices

<table>
<thead>
<tr>
<th>Severity of symptoms</th>
<th>Treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>All cases</td>
<td>Liberal intake of clear fluids. Oral rehydration salts for young children, elderly people, and travellers with medical comorbidities</td>
</tr>
<tr>
<td>Mild symptoms (1-2 unformed stools per 24 hours)</td>
<td>Loperamide: 4 mg taken immediately, then 2 mg for each loose stool to a maximum of 16 mg per day</td>
</tr>
<tr>
<td>Moderate symptoms:</td>
<td></td>
</tr>
<tr>
<td>South and Central America, Africa</td>
<td>Ciprofloxacin: 500 mg twice daily for three days</td>
</tr>
<tr>
<td>South and South East Asia</td>
<td>Azithromycin: 1 g single dose, or 500 mg daily for three days</td>
</tr>
<tr>
<td></td>
<td>Rifaximin: 200 mg three times daily for three days</td>
</tr>
<tr>
<td>High fever, severe abdominal pain, bloody diarrhoea</td>
<td>Seek local medical assistance</td>
</tr>
<tr>
<td></td>
<td>Avoid loperamide</td>
</tr>
</tbody>
</table>
High risk countries: **Asia and Africa**

- Invasive diarrhea: First choice FQ – loperamide

> Seek medical help when > 48 hours

- When treatment prescribed?
Swiss Guidelines

Swiss guidelines are unchanged since 2013

• No treatment in all types of TD
• Exceptions:
  - very isolated travel locations
  - medical antecedents (immunodeficiency and IBD)

• First choice: FQ
  Azithro indicated when travelling to Asia
Dutch Guidelines

- Symptomatic treatment – No antibiotics

- Measures in travelers with special needs
  Visit a local doctor for severe diarrhea in < 2 years and > 70 years

- AB in some groups
  Adventure travel - Chronic diseases - Immune disorders
Dutch Guidelines

Figuur 1 Schema antibiotische behandeling (AB) van acuut ontstane reizigersdiarree bij reizigers van 16 jaar en ouder

- Reizigersdiarree
  - Voorkom uitdroging
    - Reizen onder primitieve omstandigheden
    - Bepaalde onderliggende aandoeningen
      - Start AB bij diarree met koorts ± bloedbijnenging, diarree met hevige buikkrampen of bij diarree > 48 uur
        - Ciprofloxacine 3d of Azitromycine 3d
        - Indien de diarree na 1 dag gestopt is mag de kuur gestaakt worden
    - Ernstige afweerstoornis
      - Start AB na 1e ongevormde onttasting
        - Ciprofloxacine 5d of Azitromycine 3d
        - Kuur afmaken
    - Hiv CD4 cellen 200-500/mm³
      - Start AB bij slijm & bloed of na 2 dagen
        - Ciprofloxacine 5d of Azitromycine 3d
        - Kuur afmaken

* DM, renal, cardial

** Cellular and humoral deficiencies
Hypoglobulinemie
Nefrotic syndrome
Immunosuppressiva, hematological malignancies, HIV
CD4 < 200
Review of ISTM expert group:

- Mild > no antibiotics
- Serious illness > AB should be used
- Moderate? ‘AB may be used’

When inconvenience > Seek medical advice!
To summarize

- Some GI diseases are decreasing: Hepatitis A – Typhoid fever
- Some are increasing: resistance for FQ in Salmonellosis in Africa (ProMed June 2016)
- We probably prescribe too much AB for BE travellers
- Most prescribed AB are not used
- **AB effect in TD is probably overestimated in clinical effect or on effect of ‘inconvenience’**
- For Africa/South America travelers receive prescriptions for fluoroquinolones > the next year, they travel to Asia and will keep the old box of antibiotics of fluoroquinolones for his trip to Asia!
To summarize

• Reduce AB prescriptions to avoid ESBL
• Fluoroquinolone use predispose for new Salmonellosis and Campylobacter infections
• Shift to macrolides
• Scope on severe diarrhea
• Which continents have the highest risk?
• Target vulnerable patients

• Keep it simple and uniform
Travellersdiarrhea

Ce schéma doit seulement être utilisé en voyage en cas d'urgence. Ne l'utilisez pas après le retour en Belgique, mais consultez d'abord votre médecin!

Gardez l'antibiotique soigneusement et utilisez-le seulement comme traitement de secours pendant votre prochain voyage. Contrôlez la date de péremption; un produit périmé doit être emporté chez votre pharmacien.

Maar het antibioticum zorgvuldig en gebruik het uitsluitend als noodbehandeling tijdens een volge...
Selftreatment
Travelers’ Diarrhea

In serious illness: AB should be used

Diarrhea with alarming symptoms
Loose stools 3x / 24 hours
And
Or + fever 38,5°C
Or + pus in stools
Or + blood in stools
Or + heavy abdominal cramps
Travelers diarrhea

Limiting the use of standby AB in BE anno 2016

When to prescribe?

Standard guideline:
• Only for travel to Asia and Africa (not to the Americas)
  AND
• Travel more than 16 days

What to prescribe?
Only azithromycine 1 g (2 pills of 500 mg at once)
Travelers diarrhea

Limiting the use of standby AB in BE anno 2016

Only azithromycin 1 g (2 pills of 500 mg at once)

Double blind
N = 108 Intervention
N = 109 Control

Azithromycin Found to Be Comparable to Levofloxacin for the Treatment of US Travelers with Acute Diarrhea Acquired in Mexico

CID 2003
Selftreatment
Travelers’ Diarrhea

Frequent liquid diarrhea

Intake of enough solutions with salt and sugar

Loperamide 2 mg if necessary
Selftreatment
Travelers’ Diarrhea

Diarrhea with alarming symptoms
Fever – Cramps – Blood and/or Pus

AND

Travel to Asia or Africa
Travel duration ≥ 16 days

Intake of enough solutions
+ Azithromycine 1000 mg
Travelers diarrhea

When you can prescribe antibiotics?

The Exceptions

- **Adventurous travel** (longterm travel, high altitude and jungle trekking)
- **All travel to the Indian subcontinent**
- **Immunocompromised patients** (hypo- (a)globulinemie, immunosuppressiva, hematological malignancies, HIV, etc)
- **Patients with underlying disorders at risk for complications** (diabetes, renal insufficiency, heart failure, etc)
- **Children** (till 12 years)
- **Pregnancy**

PPI need to be decreased or if possible avoided during travels to tropical countries
### Selftreatment

#### Travelers’ Diarrhea

**Diarrhea with alarming symptoms**

When antibiotics?

**AND**

- Travel to Asia en Africa
- Travel duration of ≥ 16 days

### Exceptions:

- Kids (< 12 years) - Pregnancy
- Immunocompromised patients (hypo- (a)globulinemie, immunosuppressiva, hematological malignancies, HIV, etc)
- Patients with underlying disorders at risk for complications (diabetes, renal insufficiency, heart failure, etc)
- Adventurous travelers (trekking – jungle – high altitude – long duration)
- All travel to the Indian subcontinent
Example 1

• Patient with diabetes type 2 traveling to Bali for 13 days
• Prescribe azithromycine 1 g
Example 2

- Patient on methotrexate traveling to Costa Rica for 14 days
- Prescribe azithromycine 1 g
Example 3

- Trekking in Amazone for 10 days
- Prescribe Azithromycine 1 g
Example 4

- 5-year old child traveling to Africa for 8 days
- Prescribe azithromycin 10 mg/kg/day at once for three days!
Example 5

• Honeymoon to Botswana for 12 days
• Don’t prescribe antibiotics
Program

• Yellow Fever
• Travelers diarrhea
• Zika
• The pregnant traveler
• Malaria
• Other topics
AVIS DU CONSEIL SUPERIEUR DE LA SANTE N° 9340

Réponses aux questions du Risk Management Group relatives à l’actuelle épidémie de Zika et recommandations aux différents groupes de voyageurs se rendant dans des régions où sèvit une épidémie de virus Zika : état des lieux au 25 avril 2016.

In this scientific advisory report on public health policy, the Superior Health Council of Belgium provides the Belgian health authorities with specific recommendations on the prevention of Zika-virus infections in individuals travelling to the epidemic areas and on the management of exposed travelers upon their return.

Version validée par le Collège de Mai 2016

ADVIES VAN DE HOGE GEZONDHEIDSRAAD nr. 9340

Antwoorden op de vragen van de Risk Management Group i.v.m. de huidige zika-epidemie en aanbevelingen voor de verschillende reizigersgroepen die naar gebieden reizen waar een zika-epidemie woedt. Stand van zaken op 25 april 2016

In this scientific advisory report on public health policy, the Superior Health Council of Belgium provides the Belgian health authorities with specific recommendations on the prevention of Zika virus infections in individuals travelling to the epidemic areas and on the management of exposed travelers upon their return.

Versie gevalideerd op het College van Mei 2016
Transmission

• Mainly through Aedes mosquitoes
• But also:
  – mother-child during pregnancy
  – Bloodtransfusion
  – Sexual contact: man-woman and man-man
    • But how long is semen infectious?
    • What about asymptomatic patients?
    • How long to wait before conception?
WHO and CDC:

<table>
<thead>
<tr>
<th></th>
<th>Women</th>
<th>Men</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Zika symptoms</strong></td>
<td>At least 8 weeks after symptoms start</td>
<td>At least 6 months after symptoms start</td>
</tr>
<tr>
<td><strong>No Zika symptoms</strong></td>
<td>At least 8 weeks after return from visit</td>
<td>At least 8 weeks after return from visit</td>
</tr>
</tbody>
</table>

But how sure are we that 8 weeks is long enough ????
Rapid Communications

Sexual transmission of Zika virus in an entirely asymptomatic couple returning from a Zika epidemic area, France, April 2016

T Fréour 1, S Mirallié 1, B Hubert 2, C Splingart 1, P Barrière 1, M Maquart 4, I Leparc-Goffart 4

Correspondence

Late sexual transmission of Zika virus related to persistence in the semen day 53 and a semen sample obtained on day 67 since symptom onset were both negative for Zika virus RNA by RT-PCR. The woman had no symptoms during the trip to Martinique, 40 days during sex for 1 month after their return—should be extended, especially in the case of sexual intercourse involving women of reproductive age.

44 days post symptoms
<table>
<thead>
<tr>
<th>Population</th>
<th>Avant voyage</th>
<th>Durant séjour</th>
<th>Au retour</th>
</tr>
</thead>
<tbody>
<tr>
<td>Femme enceinte</td>
<td>Voyage déconseillé toute la grossesse</td>
<td>Interrompre le séjour ou si séjour indispensable,</td>
<td>Poursuivre abstinence ou rapports sexuels protégés jusqu'à prise en charge par un expert².</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td><strong>En cas de symptômes d'infection actifs/récents:</strong></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>- PCR² sérum et/ou urine (IMT⁴), à combiner avec test sérologique de screening ELISA Zika IgM/IgG (IMT) sur sérum convalescent</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>- Si PCR négatif et test sérologique positif, confirmation avec VNT⁵ (IMT)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td><strong>En cas de symptômes résolus ou si asymptomatique</strong></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>- Test sérologique de screening ELISA Zika IgM/IgG (IMT) 3 semaines après le retour (IMT)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>- Si test sérologique positif, confirmation avec VNT (IMT).</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td><strong>Si PCR ou VNT positifs, évaluation/suivi par un gynécologue/obstétricien, en lien avec un centre universitaire ou de référence en diagnostic prénatal</strong></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>- Échographie fœtale toutes les 3-4 semaines</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>- PCR liquide amniotique si anomalies échographiques suggestives d'infection par Zika</td>
</tr>
</tbody>
</table>
Program

- Yellow Fever
- Travelers diarrhea
- Zika
- The pregnant traveler
- Malaria
- Other vaccinations
Pregnant/breastfeeding travellers: what has changed?
## Malaria prophylaxis

<table>
<thead>
<tr>
<th>Pregnant</th>
<th>WHO</th>
<th>CDC</th>
<th>UK</th>
<th>French</th>
</tr>
</thead>
<tbody>
<tr>
<td>mefloquine</td>
<td>ok</td>
<td>ok</td>
<td>ok</td>
<td>ok</td>
</tr>
<tr>
<td>doxycycline</td>
<td>no</td>
<td>no</td>
<td>ok till w15</td>
<td>ok in 1st trimester</td>
</tr>
<tr>
<td>atovaquone/proguanil</td>
<td>only when high risk</td>
<td>No data, not recommended</td>
<td>Ok in 2nd and 3rd trimester</td>
<td>ok</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Breastfeeding</th>
<th>WHO</th>
<th>CDC</th>
<th>UK</th>
<th>French</th>
</tr>
</thead>
<tbody>
<tr>
<td>mefloquine</td>
<td>ok</td>
<td>ok</td>
<td>ok</td>
<td>ok</td>
</tr>
<tr>
<td>doxycycline</td>
<td>no</td>
<td>ok when shortterm use</td>
<td>ok when no alternative; max 1 w</td>
<td>ok when no alternative</td>
</tr>
<tr>
<td>atovaquone/proguanil</td>
<td>No data, not recommended</td>
<td>ok when infant &gt; 5kg</td>
<td>ok</td>
<td>ok when infant &gt; 5kg</td>
</tr>
</tbody>
</table>
# Malaria prophylaxis

<table>
<thead>
<tr>
<th>Pregnant</th>
<th>WHO</th>
<th>CDC</th>
<th>UK</th>
<th>French</th>
</tr>
</thead>
<tbody>
<tr>
<td>atovaquone/proguanil</td>
<td>only when high risk</td>
<td>No data, not recommended</td>
<td>Ok in 2nd and 3rd trimester</td>
<td>ok</td>
</tr>
</tbody>
</table>

**BE Consensus**

Atovaquone / Proguanil may be used in the pregnant traveler
Malaria treatment during pregnancy

Four Artemisinin-Based Treatments in African Pregnant Women with Malaria

The PREGACT Study Group*

3428 women; Artemisinine based treatments are safe and effective in 2nd and 3rd trimester
Malariatreatment during pregnancy

- Quinine + clindamycine
- Artemisinine based treatment (Riamet®/Eurartesim®): ok from 2nd trimester, exceptionnaly from 1st trimester when no other options are available (possibly teratogenic)
- Mefloquine: rarely used because of side effects
- Atovaquone/proguanil: few data, if no other options
- Chloroquine: ok
- Primaquine: no
Yellow fever vaccination

• **During pregnancy:**
  – WHO, CDC, Le Crat: *Pregnant women who must travel to areas where YFV exposure is likely should be vaccinated.*
  – CAVE: lower seroconversion late in pregnancy → booster to be given before next travel

• **YF vaccin en lactation:**
  – Ok when infant > 6m
  – Interrupt lactation during 2 weeks when infant < 6 months (risk of encephalitis in infant)
Program

• Yellow Fever
• Travelers diarrhea
• Zika
• The pregnant traveler
• Malaria
• Other vaccinations
• No major changes; no surprises
• Malaria prevalence is still declining worldwide (WHO malaria report 2015)
ABCD E
of malaria prevention for travelers

• **A**: Awareness
• **B**: Bite prevention
• **C**: Chemoprophylaxis, if indicated.
• **D**: Diagnosis: swift diagnosis
• **E**: Environment: Avoid outdoor activities in environments that are mosquito breeding places, especially in late evenings and at night.
Mosquito bite prevention

- Kits for self impregnation of mosquito nets (permethrine) no longer available in Belgium (except for other purposes) and thus not recommended.
WHO recommended long-lasting insecticidal nets

<table>
<thead>
<tr>
<th>Product name</th>
<th>Product type</th>
<th>Status of WHO recommendation</th>
<th>Status of publication of WHO specification</th>
</tr>
</thead>
<tbody>
<tr>
<td>DawaPlus 2.0</td>
<td>Deltamethrin coated on polyester</td>
<td>Interim</td>
<td>Published</td>
</tr>
<tr>
<td>Duranet</td>
<td>Alpha-cypermethrin incorporated into polyethylene</td>
<td>Full</td>
<td>Published</td>
</tr>
<tr>
<td>Interceptor</td>
<td>Alpha-cypermethrin coated on polyester</td>
<td>Full</td>
<td>Published</td>
</tr>
<tr>
<td>LifeNet</td>
<td>Deltamethrin incorporated into polypropylene</td>
<td>Interim</td>
<td>Published</td>
</tr>
<tr>
<td>MAGNet</td>
<td>Alpha-cypermethrin incorporated into polyethylene</td>
<td>Full</td>
<td>Published</td>
</tr>
<tr>
<td>MiraNet</td>
<td>Alpha-cypermethrin incorporated into polyethylene</td>
<td>Interim</td>
<td>Published</td>
</tr>
<tr>
<td>Olyset Net</td>
<td>Permethrin incorporated into polyethylene</td>
<td>Full</td>
<td>Published</td>
</tr>
<tr>
<td>Olyset Plus</td>
<td>Permethin and PBO incorporated into polyethylene</td>
<td>Interim</td>
<td>Published</td>
</tr>
<tr>
<td>Panda Net 2.0</td>
<td>Deltamethrin incorporated into polyethylene</td>
<td>Interim</td>
<td>Published</td>
</tr>
<tr>
<td>PermaNet 2.0</td>
<td>Deltamethrin coated on polyester</td>
<td>Full</td>
<td>Published</td>
</tr>
<tr>
<td>PermaNet 3.0</td>
<td>Combination of deltamethrin coated on polyester with strengthened border (side panels), and deltamethrin and PBO incorporated into polyethylene (roof)</td>
<td>Interim</td>
<td>Published</td>
</tr>
<tr>
<td>Royal Sentry</td>
<td>Alpha-cypermethrin incorporated into polyethylene</td>
<td>Full</td>
<td>Published</td>
</tr>
<tr>
<td>SafeNet</td>
<td>Alpha-cypermethrin coated on polyester</td>
<td>Full</td>
<td>Published</td>
</tr>
<tr>
<td>Yahe</td>
<td>Deltamethrin coated on polyester</td>
<td>Interim</td>
<td>Published</td>
</tr>
<tr>
<td>Yorkkool</td>
<td>Deltamethrin coated on polyester</td>
<td>Full</td>
<td>Published</td>
</tr>
</tbody>
</table>

None of them is available in Belgium
Which repellents?

• **DEET:**
  • 40-50% for traveller
  • for pregnant and children: 20-30% (1/d)

• **Les well documented-non DEET:**
  – (p)icaridine:
    • Ok for children > 2y
    • Ok for pregnant women <25%
  – **IR3535** (exists in long lasting formulation 35%, duration of activity close to DEET
    • Ok for children <2y with formulation <25%
    • Ok for pregnant with <25%
  – **PMD**: short duration of activity
    • not for pregnant

Based on BEH
Which strategies exist in low malaria risk areas?

**GERMAN SPEAKING EUROPE**
- Bite prevention always
- **AND** think of malaria when sick
- Standby emergency treatment

**BELGIUM**
- Bite prevention always
- **AND** think of malaria when sick
- Chemoprophylaxis when risk is locally/circumstances higher
- (SBET in some cases)
Figure 2.5 Estimated *P. falciparum* infection prevalence among children aged 2–10 years (*PfPR*<sub>2–10</sub>) in 2000 and 2015

API, annual parasite index; *PfPR*, *P. falciparum* parasite rate
Source: Malaria Atlas Project (18)
WHO malaria report 2016:

• Elimination= no indigenous malaria cases for 3 consecutive years

• For the first time ever: no indigenous cases in Europe
2.5 Towards elimination of malaria in the WHO European Region

The WHO European Region reported zero indigenous cases for the first time in 2015, in line with the goal of the Tashkent Declaration to eliminate malaria from the region by 2015. The region comprises 53 countries and covers the European Union as well as the Balkan countries, the Russian Federation, Israel, Turkey and countries in South Caucasus and Central Asia. In 1975, the WHO

Figure 2.9 Indigenous malaria cases in the WHO European Region, by country, 1990–2015

Source: National malaria control programme reports and WHO estimates
### Table 2.6 Classification of countries by programme phase, December 2015

<table>
<thead>
<tr>
<th>WHO region</th>
<th>Pre-elimination</th>
<th>Elimination</th>
<th>Prevention of reintroduction</th>
<th>Malaria free</th>
</tr>
</thead>
<tbody>
<tr>
<td>African</td>
<td>Cabo Verde</td>
<td>Algeria</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Americas</td>
<td>Dominican Republic</td>
<td>Argentina, Belize, Costa Rica, Ecuador, El Salvador, Mexico, Paraguay</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Eastern Mediterranean</td>
<td>Iran (Islamic Republic of), Saudi Arabia</td>
<td>Egypt, Iraq, Oman, Syrian Arab Republic</td>
<td>Morocco – 2010, United Arab Emirates – 2007</td>
<td></td>
</tr>
<tr>
<td>European</td>
<td>Turkey, Tajikistan</td>
<td>Azerbaijan, Georgia, Kyrgyzstan, Uzbekistan</td>
<td>Turkmenistan – 2010, Armenia – 2012</td>
<td></td>
</tr>
<tr>
<td>South-East Asia</td>
<td>Bhutan, Democratic People's Republic of Korea</td>
<td>Sri Lanka</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Western Pacific</td>
<td>Malaysia</td>
<td>China, Republic of Korea</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Source: National malaria control programme data

- **Mosquito bite prevention**
- **Mosquito bite prevention**
- **No preventive measures**
Malaria 2015 (source WHO 2010, World Malaria Report 2014)

Map showing areas of infection risk with labels A, B, and C indicating different types of interventions:
- A: Mosquito bite prevention only
- B: Nivaquine® weekly
- C: Malarone® or doxycycline daily; Lariam® weekly

For details, see www.itg.be
Malaria 2016  (source WHO 2010, World Malaria Report 2015)
SOME EXAMPLES...
BUT NO MAP IS 100% CORRECT....
Ecuador

• Er is **geen malariarisico** in de gebieden gelegen **boven 1500 m** (Andes gebergte in het centrale en het zuidelijke gedeelte van het land), in de **grote steden** (o.a. Quito, Guayaquil, de steden in het Andesgebied), noch op de **Galapagos-eilanden**.

• Er is **weinig malariarisico** in de lager gelegen gebieden **<1500 m ten westen van de Andes** aan de Stille Oceaan. Antimugmaatregelen (*) tussen valavond en ochtend zijn aanbevolen.

• Er is een **laag risico** in het **Amazonegebied** ten oosten van de Andes. Antimugmaatregelen (*) tussen valavond en ochtend zijn aanbevolen. Enkel bij een verblijf in afgelegen plattelandsgebieden waar men zich ’s avonds en ’s nachts blootstelt aan muggen (zoals bij een langdurige jungle trekking) kan men de inname van malariatabletten (**) overwegen.
Equateur

• Il n’y a **pas de risque** de malaria dans les régions situées au-dessus de 1500 m (*Andes*, la chaîne montagneuse dans le centre et dans le sud du pays); et pas non plus dans les **grandes villes** (e.a. Quito, Guayaquil et les villes de la région des Andes), ni dans les **îles Galapagos**.

• Il y a un **risque faible** de malaria dans la région en **dessous de 1500 m à l’est des Andes** (côté de l’Océan Pacifique). Des mesures antimoustiques (*) sont recommandées.

• Il y a un **risque faible** dans la **zone amazonienne** à l’est des Andes. Des mesures antimoustiques (*) sont recommandées. Seulement pour les voyages très aventureux dans des régions très éloignées où l’on passe ses soirées et ses nuits exposé aux moustiques (comme un trekking dans la jungle de longue durée), on peut parfois opter pour une **chimioprophylaxie (**)**.
Myanmar (Birma)
Er is geen malariaisico

- in de stedelijke gebieden (Yangon (Rangoon), Mandeley, Naypyidaw de nieuwe hoofdstad).
- In het kustgebied, behalve in Rahkine (noordelijke deel van de kustlijn).
- In de hoogplateaus > 1000 m (oa Shan plateaus in het noordoosten met het Inlé meer, Tenasserim in het zuiden thv de grens met Thailand, Naga hills in het noordwesten)

Hier zijn geen preventieve maatregelen nodig.

Er is weinig tot matig malariaisico in de rest van het land:

- Rahkine (noordelijke deel van de kustlijn)
- Lager gelegen gebieden < 1000 m in het centrum en het zuidoosten van het land (oa Bahan)

Antimugmaatregelen (*) tussen valavond en ochtend zijn aanbevolen voor de meeste reizen. Enkel bij een verblijf in afgelegen plattelandsgebieden waar men zich ’s avonds en ’s nachts blootstelt aan muggen kan men de inname van preventieve malariatabletten overwegen (**).

Aan de grens met Thailand, Laos en China is er resistentie tegen mefloquine.
Il n’y a **pas de malaria**

- Dans les **régions urbaines** (comme Yangon (Rangoon), Mandeley, Naypyidaw-la nouvelle capitale)
- **La côte**, sauf l’état de Rahkine (partie nord de la côte)
- Dans les **haut-plateaux > 1000 m** (entre autre le plateau de Shan dans le nord-est avec le Lac Inlé, Naga Hills dans le nord-ouest, Tenasserim Hills dans le sud à la frontière avec la Thaïlande)

Aucune mesure préventive n’est nécessaire pour se protéger contre la malaria dans ces régions.

Il y a **un risque faible/ modéré** de malaria dans le reste du pays :
- Rahkine
- **Les zones < 1000 m** au centre et au sud-est du pays (entre autre le site de Bahan)

Pour la plupart des voyages touristiques, des mesures antimoustiques (*) sont suffisantes. Pour les voyages dans des régions très éloignées où l’on passe ses soirées et ses nuits exposés aux moustiques, on peut opter pour une chimioprophylaxie (**). A la frontière avec la Chine, la Thaïlande et le Laos, il y a une résistance contre la mefloquine.
Indonesia
Indonesia

Figure 2. Annual Parasite Index (API) per province and compared with country total API, 2013 (data from Indonesian MoH).

There is no risk of malaria on Java, Bali and in the big cities of all Indonesian islands (except Papua & West Papua). Precautions against malaria are not necessary.

There is little to moderate risk of malaria on Sumatra, Lombok, South-Kalimantan (South Borneo), South-West-, West- and Central-Sulawesi (the whole of Sulawesi, except for the extreme north and eastern extension) and Gili-islands (between Bali and Lombok). Prevention against mosquito bites between dusk and dawn is recommended (*). Only when travelling in rural areas where one might be exposed to mosquitos in the evening or at night, one can opt for malaria prophylaxis (**)

There is a high risk of malaria on North-Sulawesi and South-East Sulawesi, North - and Central Kalimantan (Borneo), Papoea and West-Papoea (Irian Jaya), and on all islands east of Lombok/Gili islands (Sumba, Flores, Sumbawa, Timor, Molukes and others). Prevention against mosquito bites (*) and malaria pills (**) are recommended.
Philippines
• Il n'y a pas de risque de malaria dans les villes (ea à Manille), ni dans les îles au centre (Visayas, sauf Palawan), ni dans les régions situées au-dessus de 600 m.

• Il y a un risque faible de malaria dans les régions rurales situées en dessous de 600 m de Luzon (la grande île au nord), Mindoro (au sud de Luzon), Mindanao (la grande île au sud), Basilu, Sulu et Tawi-Tawi (les petites îles à l’ouest de Mindanao). Pour la plupart des voyages touristiques, des mesures anti-moustiques sont suffisantes (*). Pour les voyages dans des régions très éloignées où l’on passe ses soirées et ses nuits exposé aux moustiques, on peut opter pour une chimioprophylaxie (**).

Il y a un risque modéré de malaria à Palawan (l’île allongée au sud ouest). Des mesures antimoustiques (*) et une chimioprophylaxie (**) sont recommandées.
Filipijnen

- Er is geen malarialisico in de steden (oa Manilla), de centraal gelegen eilanden (Visayas behalve Palawan) en in de gebieden gelegen boven de 600 m. Er zijn geen preventieve maatregelen nodig.

- Er is weinig malarialisico in de lager gelegen (<600 m) rurale gebieden van Luzon (het grote eiland in het noorden), Mindoro (ten zuiden van Luzon), Mindanao (grote eiland in het zuiden), Basilu, Sulu en Tawi Tawi (kleine eilandjes ten westen van Mindanao). Voor de meeste toeristische reizen volstaan antimugmaatregelen (*) tussen valavond en ochtend. Enkel bij een verblijf in afgelegen plattelandsgebieden waar men zich ’s avonds en ’s nachts blootstelt aan muggen kan men de inname van preventieve malariatabletten (**) overwegen.

- Er is een matig malarialisico in Palawan (lange eiland in het westen). Antimugmaatregelen tussen valavond en ochtend (*) en de inname preventieve malariatabletten zijn aanbevolen (**).
Questions?

What about the use of atovaquone/proguanil 2/week?

> Not enough evidence
Program

• Yellow Fever
• Travelers diarrhea
• Zika
• The pregnant traveller
• Malaria
• Other topics, mostly vaccination-related
# Routine vaccinations

<table>
<thead>
<tr>
<th>Vaccines</th>
<th>8 WEEKEN</th>
<th>12 WEEKEN</th>
<th>16 WEEKEN</th>
<th>12 MAAND</th>
<th>13 MAAND</th>
<th>15 MAAND</th>
<th>18 MAAND</th>
<th>5-7 JAAR</th>
<th>10-13 JAAR</th>
<th>14-16 JAAR</th>
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<tr>
<td>Poliomyelitis²</td>
<td>IPV</td>
<td>IPV</td>
<td>IPV</td>
<td>IPV</td>
<td>IPV</td>
<td>IPV</td>
<td>IPV</td>
<td>dTPa</td>
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<td></td>
</tr>
<tr>
<td>Difterie Tetanus Kinkhoest⁶</td>
<td>DTPa</td>
<td>DTPa</td>
<td>DTPa</td>
<td>DTPa</td>
<td></td>
<td></td>
<td></td>
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<td></td>
<td></td>
</tr>
<tr>
<td>Haemophilus influenzae type b⁴</td>
<td>Hib</td>
<td>Hib</td>
<td>Hib</td>
<td>Hib</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>2003</td>
</tr>
<tr>
<td>Hepatitis B²</td>
<td>HBV</td>
<td>HBV</td>
<td>HBV</td>
<td>HBV</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mazelen Bof Rubella³</td>
<td></td>
<td></td>
<td></td>
<td>MBR₁</td>
<td>MBR₂</td>
<td>MBR₂</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Meningokok C'⁴</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>1985</td>
<td></td>
<td>MenC</td>
<td>1995</td>
<td></td>
</tr>
<tr>
<td>Pneumokok³</td>
<td>Pn7V</td>
<td>Pn7V</td>
<td>Pn7V</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Rotavirus³</td>
<td>ROTA</td>
<td>ROTA</td>
<td>ROTA</td>
<td>(ROTA)</td>
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<td></td>
<td></td>
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<td>HPV¹³</td>
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<td></td>
</tr>
</tbody>
</table>

**Gecomбинeerd Vaccin.**

**Vaccinatiestoestand nagaan en indien nodig aanvullen.**

**1ère en 2ste dosis MBR vaccin.**

**N.B.:** er bestaat een internationale afspraak om met de hoofdletters “D” en “P” te verwijzen naar de pediatrische dosis voor difterie en kinkhoest, terwijl de kleine letters “d” en “p” verwijzen naar de lagere dosis difterie en kinkhoest voor volwassenen.
Tetanos and diphteria

• Before travel = ideal moment to double check
  – Tetanos
  – Diphteria

• One booster vaccination every 10 years:
  Tedivax pro adulto®
  Revaxis® (+ polio)
  Boostrix® - Boostrix- polio® (+ pertussis and polio)
Een kleuter van 3 jaar is afgelopen nacht overleden aan de gevolgen van difterie in het Universitair Ziekenhuis van Antwerpen. Het meisje was sinds 10 maart opgenomen in het ziekenhuis. Het is nog onduidelijk hoe het kind besmet is geraakt.
Measles-Mumps-Rubella

- The trivalent vaccin (+ mumps + rubella) administered in BE since **1985**.
- A second injection is necessary at the age of 12 years since **1995**.
- Persons born before **1970** have probably antibodies.

Don’t combine booster vaccination with yellow fever vaccination
> wait at least 4 weeks!
Hepatitis A vaccins

• **Hepatitis A**
  • **Havrix 720° Junior** (1-15j)
  • **Havrix 1440°** Adult
    Schema: IM  M₀ – M₆-₁₂
  
• **Vaqta 50°**
• **Vaqta 25 Junior° (1-17j)**

• **Hepatitis A + B**
  • **Twinrix °**: contains only 720 IU hep A
  • M₀ - M₁ - M₆ à 12
  • always 2 Hep A vaccines before departure
Hepatitis B

- Since 1986 routine vaccination
- Risk depends on risk behaviour
- All expats/health care workers should be vaccinated
- Check Ab titer; if > 10 U/ml: lifelong protection

Schema: M0-M1-M6 = 91-95 % & lifelong
Other vaccinations

Hepatitis B

Off-label vaccine dosing: accelerated schedules

Faster vaccine schedules: Hepatitis A-B IM

(d0 > m1 > m4-6)  IM d0 - d7 - d21 - d365

Figure 2  Seroprotection associated with an accelerated regimen of recombinant hepatitis B vaccine. (Reprinted with permission from J Travel Med.)


Other vaccinations

Hepatitis B

Off-label vaccine dosing: accelerated schedules

Faster vaccine schedules: Hepatitis A-B IM

(d0 > m1 > m4-6)  IM d0 - d7 - d21 - d365

N= 479

Control

N= 239

N= 240

Other vaccinations

Hepatitis B

Off-label vaccine dosing: accelerated schedules

Faster vaccine schedules: Hepatitis A-B IM

(d0 > m1 > m4-6) → IM d0 - d7 - d14

<table>
<thead>
<tr>
<th>BE Defense</th>
<th>N</th>
<th>Antibodies Hep BsAB after booster 12 m</th>
</tr>
</thead>
<tbody>
<tr>
<td>Engerix D0-7-14</td>
<td>38</td>
<td>94%</td>
</tr>
<tr>
<td>Twinrix D0-7-14</td>
<td>45</td>
<td>96%</td>
</tr>
</tbody>
</table>

Soentjens Unpublished data
Other vaccinations

**Polio**

Extra polio vaccination is **mandatory** for people who have stayed at least 4 weeks in a country where wild polio virus is circulating:

- Pakistan
- Afghanistan

Extra polio vaccination is **strongly recommended** for people leaving countries where vaccine derived polio virus is circulating:

- Ukraine
- Madagascar
- Nigeria
- Guinée
- Laos - Myanmar
### States currently exporting wild poliovirus or cVDPV

- Afghanistan
- Pakistan

### States infected with wild poliovirus or cVDPV but not currently exporting

- Guinea
- Lao People's Democratic Republic
- Madagascar
- Myanmar*
- Nigeria
- Ukraine

### States no longer infected by wild poliovirus or cVDPV, but which remain vulnerable to international spread, and states that are vulnerable to the emergence and circulation of VDPV

- Cameroon
- Equatorial Guinea
- Ethiopia
- Iraq
- Israel
- Somalia
- South Sudan
- Syrian Arab Republic

Extra vaccine is mandatory

Extra vaccine is recommended

http://www.polioeradication.org/Home.aspx
• Aim: avoiding reintroduction of poliovirus in countries free of polio

• For travellers staying at least 4 weeks (and residents)
  – Extra vaccine needs to be administered between 4 weeks and 12 months before leaving the country where polio is present
  – International health regulations account for countries where polio is circulating and exported: (Afghanistan and Pakistan): proof of vaccination in yellow booklet (pages 4-5)

• Possible vaccines:
  – Imovax® Polio
  – Revaxis®
  – Boostrix-Polio®
  – Tetravac®
  – Infanrix-IPV®
  – Hexyon®
  – Infanrix-Hexa®
Typhoid fever

- Vaccination is indicated for travel **longer than 3 weeks** to the **Indian subcontinent**
- Vaccination can be considered for **adventurous travel** to the (sub)tropics in poor hygienic circumstances and for migrants and their children (**VFR**)  
- Subjects with met a- of hypochlorhydrie have increased risk
Other vaccinations

• **Typhim® en Typherix®**
  - SC D0, booster after 3y
  - >2y

• **Hepatyrix®**
  - S typhi+ Hep A (1440 IE)
  - D0- 6/12m
  - > 15y

(Vivotif) ® life attenuated
Not on the BE market
D0 – D3 – D6 nuchter – booster after 3 y
>5y
Meningcoccal disease

- **Mandatory** for Mekka pelgrimage (Umrah and Hajj)
  - only 3 years validity (following the Saudi-Arabia authorities)
  - Normal validity after a conjugate vaccination = 5 years

8 years to be confirmed  

- **Advised** during dry season in “meningitis belt” (december-june)
  - For travellers in close contact with local population
  - Travelers staying at least 4 weeks
Meningokokkenvaccin
ACW$_{135}Y$

- **Nimenrix**
  - Conjungated vaccine
  - against Meningococcus A C W135Y
  - > 1 y old
  - 5 year valid, except for pelgrimage: only 3 y
  - Vaccination at least 10 days before departure

- **Menveo**
  - Conjungated vaccine
  - against Meningococcus A C W135Y
  - > 2 y old
  - 5 year valid, except for pelgrimage: only 3 y
  - Vaccination at least 10 days before departure
Influenza

“1000/100.000/ month”

CDC 2009 – CLASSIC ADVICE

Influenza vaccine should be recommended before travel for persons at high risk for complications of influenza if

1) influenza vaccine was not received during the preceding fall or winter,
2) travel is planned to the tropics,
3) travel is planned with large groups of tourists at any time of year,
4) travel is planned to the Southern Hemisphere from April through September.

In the Northern Hemisphere, travel-related influenza vaccination should take place by spring when possible, because influenza vaccine may not be available during the summer.
Other vaccinations

Zones de circulation du virus de l’encéphalite à tiques et des tiques vectrices (données valables au 31 mai 2016)

Source: TBE Europe: http://www.tbe-europe.com; Fond de carte ESRI, 2000; InVS, 2013
Other vaccinations

Tick borne encephalitis

- **FSME junior®** - (Encepur junior®) (0.25ml) van 1-16j
- **FSME Adult®** - (Encepur®) (0.5ml)

- Schema: $M_0 - M_{1-3} - M_{9-12}$
- Versneld schema: $D_0 - D_{14} - M_{5-12}$
- Booster na 3 jaar en erna om de 5 jaar
Other vaccinations

Tick Borne encephalitis

Off-label vaccine dosing: accelerated schedules

Faster vaccine schedules: Tick Borne Encephalitis

(d0 > m1-3 > m9-12 > y3 > y5) ➔

d0 > d7 > d21

d0 > d14 > d365

Tick-borne encephalitis (TBE) vaccination:
Applying the most suitable vaccination schedule

I. Schändorf, J. Beran, D. Cizkova, V. Lesna, A. Banzhoff, O. Zent

Novartis Vaccines and Diagnostics GmbH & Co. KG, Clinical Research & Medical Affairs, Emil-von-Behring-Str. 76, 35041 Marburg, Germany

Vaccination and Travel Medicine Centre, Poliklinika II., Bratislava 895, 80003 Bratislava, Czech Republic

Received 18 August 2006; accepted 18 October 2006
Available online 10 November 2006
Other vaccinations

Tick borne encephalitis

Off-label vaccine dosing: accelerated schedules

Faster vaccine schedules: Tick Borne Encephalitis
(d0 > m1-3 > m9-12 > y3 > y5)  
\[\text{d0 > d7 > d21}\]
\[\text{d0 > d14 > d365}\]

Encephalitis Vaccine Schedule N AB N AB
<table>
<thead>
<tr>
<th>Encephalitis Vaccine</th>
<th>Schedule</th>
<th>N AB Day 21</th>
<th>N AB Day 42</th>
</tr>
</thead>
<tbody>
<tr>
<td>Group R N= 66</td>
<td>D0-7-21</td>
<td>95%</td>
<td>100%</td>
</tr>
<tr>
<td>Group C N= 66</td>
<td>D0-28-300</td>
<td>76%</td>
<td>100%</td>
</tr>
<tr>
<td>Group M N= 133</td>
<td>D0-21-300</td>
<td>83%</td>
<td>98,5%</td>
</tr>
<tr>
<td>Group A N= 133</td>
<td>D0-14-300</td>
<td>99%</td>
<td>100%</td>
</tr>
</tbody>
</table>

Other vaccinations

Tick borne encephalitis

Booster vaccine schedules: Tick Borne Encephalitis

(d0 > m1-3 > m9-12 > y3) > 7 years

(d0 > m1-3 > m9-12) > 8 years

NECTM BERGEN 2014
Japanese encephalitis

Ixiaro®

Schema: IM $D_0 - D_{28}$

- first booster after 12-24 months
- 2nd booster after 6 y (or probably 10 y) more data needed
- Pediatric dose not available: $\frac{1}{2}$ adult dose for children between 2 months and 3 years

- Rapid schema (off label, but accepted in France):
  - D0-D8, booster M12-24
Japanese encephalitis

Off-label vaccine dosing: accelerated schedules

Faster vaccine schedules: Japanese encephalitis Ixiaro IM

Ixiaro (d0 > d28 > y1-2) → IM d0 - d7

Jelinek et al. TM&ID 2015.
Other vaccinations

Japanese encephalitis

Off-label vaccine dosing: accelerated schedules

Faster vaccine schedules: Japanese encephalitis Ixiaro IM

Ixiaro (d0 > d28 > y1-2) → IM d0 - d7
Japanese encephalitis

Off-label vaccine dosing: accelerated schedules

Faster vaccine schedules: Japanese encephalitis

- **Ixiaro®**
  - d0 - d7

Available only in Asia

- **CDJ Vax®**
  - Live-attenuated
  - d0 - d365
  - China Booster after one year

- **IMOJEV MD®**
  - Chimeric - Live attenuated
  - d0
  - Sanofi Pasteur
  - No booster
  - 55 dollar (Cambodja) - 47 dollar (Thailand) (personal communications)
Rabies

- Bite prevention!
- After being bitten: wash wound immediately with water and soap
- Pre-travel schedule IM: Rabipur® or HDCV®
  - D0 - D7 - D21 or D28 (no booster after 1y, no need for measuring antibodies)
  - Accelerated schema off label (d0 - d4 - d8)
  - Intradermal schema off label: lower dose needed
- Vaccination aims “boostability” lifelong, which simplifies post exposure procedure (2 extra vaccinations on d0 and d3, no immunoglobulins)
Simplifying PrEP

Rabies pre-exposure prophylaxis (PrEP)

‘Boostability’

RFFIT > 0.5 IU/ml

D0  D7  D28
PrEP X?

RISK

D365 - 1097
PEP Y?
Other vaccinations

Rabies encephalitis

Off-label vaccine dosing: accelerated schedules

Faster vaccine schedules: Rabies IM  
(IM/ID d0 > d7 > d21-28)  Rabipur IM  
IM d0 - 3 - 7

Jelinek et al. NECTM, Bergen, June 2014.  
Jelinek et al. TM&ID 2015.
Other vaccinations

Rabies encephalitis

Off-label vaccine dosing: accelerated schedules

Faster vaccine schedules: Rabies IM

(IM/ID d0 > d7 > d21-28) IM d0 - 3 - 7

Rabipur IM

Rabies Vaccine 1 ml PCECV 1 ml PCECV 1 ml PCECV

Dose 1 ml IM 1 ml IM 1 ml IM

Primary Schedule D0 1x 1 ml D0 1x 1 ml D0 1x 1 ml
D7 1x 1 ml D7 1x 1 ml D3 1x 1 ml
D28 1x 1 ml D28 1x 1 ml D7 1x 1 ml

RFFIT D35 D35 D35

Jelinek et al. TM&ID 2015.
Other vaccinations

Rabies encephalitis

Off-label vaccine dosing: accelerated schedules

Faster vaccine schedules: Rabies IM

(IM/ID d0 > d7 > d21-28)

Rabipur IM

IM d0 - 3 - 7

Jelinek et al. TM&ID 2015.
Other vaccinations

Rabies encephalitis

Off-label vaccine dosing: accelerated schedules

Faster vaccine schedules: Rabies IM
(IM/ID d0 > d7 > d21-28)

Rabipur IM
IM d0 - 3 - 7
Other vaccinations

Rabies encephalitis

Off-label vaccine dosing: accelerated schedules

Faster vaccine schedules: Rabies IM  
(IM/ID d0 > d7 > d21-28)

Rabipur IM  
IM d0 - 3 - 7

Any local solicited reactions were reported by 73% to 75% of subjects across groups, systemic reactions were observed in 60% to 66% of subjects across groups (Figure 3).

The most common local reaction after any vaccination was pain (51% to 57% across groups); the most common systemic reactions after any vaccination were fatigue (33% to 43% across groups) and headache (37% to 41% across groups). Severe reactions occurred in ≤ 3% (local) and ≤ 4% (systemic) of subjects across rabies groups.
Simplifying PrEP

Rabies pre-exposure prophylaxis (PrEP)

‘Boostability’

RFFIT > 0.5 IU/ml

PrEP X? PEP Y?

PEP after risk

D0

PrEP

RISK

D365 - 1095
Intradermal Rabies Schedules

Intradermal Rabies PrEP in BE troops

<table>
<thead>
<tr>
<th>N</th>
<th>Rabies Pre-exposure Schedule</th>
<th>RFFIT &gt;0,5IU/ml</th>
<th>GMT Median</th>
</tr>
</thead>
<tbody>
<tr>
<td>N &gt; 10.000</td>
<td>Started rabies vaccination since 2008</td>
<td></td>
<td></td>
</tr>
<tr>
<td>N = 881</td>
<td>4ID retrospectif</td>
<td><img src="#" alt="Schedule Diagram" /></td>
<td>100%</td>
</tr>
<tr>
<td>N = 489</td>
<td>3ID retrospectif</td>
<td><img src="#" alt="Schedule Diagram" /></td>
<td>82% over time</td>
</tr>
<tr>
<td>N = 250</td>
<td>3ID prospectif</td>
<td><img src="#" alt="Schedule Diagram" /></td>
<td>100%</td>
</tr>
<tr>
<td>N = 250</td>
<td>2ID prospectif</td>
<td><img src="#" alt="Schedule Diagram" /></td>
<td>100%</td>
</tr>
<tr>
<td>N = 330</td>
<td>1ID prospectif</td>
<td><img src="#" alt="Schedule Diagram" /></td>
<td>81,2% minidose</td>
</tr>
</tbody>
</table>

Future option?
Other vaccinations

• Dengue vaccine

Not indicated for travelers

Efficacy of a Tetravalent Dengue Vaccine in Children in Latin America

Luis Villar, M.D., Gustavo Horacio Dayan, M.D., José Luis Arredondo-García, M.D., Doris Maribel Rivera, M.D., Rivaldo Cunha, M.D., Carmen Deseda, M.D., Humberto Reynales, M.D., Maria Selma Costa, M.D., Javier Osvaldo Morales-Ramírez, M.D., Gabriel Carrasquilla, M.D., Luis Carlos Rey, M.D., Reynaldo Dietze, M.D., Kleber Luz, M.D., Enrique Rivas, M.D., Maria Consuelo Miranda Montoya, M.D., Margarita Cortés Supelano, M.D., Betzana Zambrano, M.D., Edith Langevin, M.Sc., Mark Boaz, Ph.D., Nadia Tornieporth, M.D., Melanie Saville, M.B., B.S., and Fernando Noriega, M.D., for the CYD15 Study Group*
Other vaccinations

• Dengue vaccine
  
  Not indicated for travelers

  • N= 10.000 (2-14 years)
    
    56,5%  50,3% - 78,4% - 75,3% (serotypes 1, 3, 4)
    
    35,5 %  DENV-naïve subjects

  • N= 20.875 (9-16 years)
    
    60,8%  50,3% - 42,3% - 74% - 77,7% (serotypes 1, 2, 3, 4)

Protection on severe disease: dengue hemorrhagic fever: 88,5% - 95,5% in both groups
Other vaccinations

• Malaria vaccine

Not indicated for travelers
Don’t forget MERS CoV
Don’t forget MERS CoV
Don’t forget MERS CoV

MERS-COV (71): SAUDI ARABIA (MAKKAH), PILGRIMAGE CAUTION, WHO

*******************************************
A ProMED-mail post
<http://www.promedmail.org>
ProMED-mail is a program of the
International Society for Infectious Diseases <http://www.isid.org>

In this update:
[1] Saudi Arabia 1 new case, 1 death, 1 recovery

*****
[1] Saudi Arabia 1 new case, 1 death, 1 recovery
Date: 23 Jun 2016
Source: Saudi MOH 22-23 Jun 2016 [edited]

As of 13:00 [1 PM] today [23 Jun 2016] there have been a total of:
1419 laboratory confirmed cases of MERS-CoV infection including
595 deaths [reported case fatality rate 41.9 percent]
791 recoveries, and
33 currently active cases [including 20 asymptomatic infections]

In the past 48 hours there has been:
1 newly confirmed case
1 newly reported fatality, and
1 newly reported recovery
Don’t forget MERS CoV

- [Fever AND pneumonia or ARDS] AND EITHER:
  - History of relevant travel within 14 days before symptom onset
  OR
  - Close contact with symptomatic traveler who developed F and ARI within 14 days after relevant travel
  OR
  - Member of a cluster of patients with severe ARI of unknown etiology in which MERS-CoV is being evaluated, in consultation
  OR
- F AND respiratory illness AND being in healthcare facility within 14 days before symptom onset in relevant geography in which recent healthcare-associated cases of MERS have been identified
  OR
- F OR respiratory illness AND close contact with confirmed case

Informatie voor deskundigen

Reizigersgeneeskunde voor de huisarts

- Train the Trainer Huisarts & reisgeneeskunde BASICS draft 25-11-2015

Consensusteksten

Consensus 2015

- Summary consensus 2015
- Brochure van de consensusvergadering van de Wetenschappelijke Studiegroep Reisgeneeskunde, onder de auspiciën van de Hoge Gezondheidsraad - sectie vaccinaties.
- Handout slides consensus 2015 – part Ia - yellow fever
- Handout slides consensus 2015 – part Ib - malaria
- Handout slides consensus 2015 – part II - other vaccinations, TD & varia

Consensus 2014

- Brochure van de consensusvergadering van de Wetenschappelijke Studiegroep Reisgeneeskunde, onder de

www.itg.be/reisgeneeskunde
## Timings

<table>
<thead>
<tr>
<th>Deliverables</th>
<th>Cycli</th>
<th>Timings</th>
</tr>
</thead>
<tbody>
<tr>
<td>CISTM</td>
<td>2 y</td>
<td>may 2017</td>
</tr>
<tr>
<td><strong>BE Seminar</strong></td>
<td>2 y</td>
<td><strong>oct 2017</strong></td>
</tr>
<tr>
<td>NECTM</td>
<td>2 y</td>
<td>Jun 2018</td>
</tr>
<tr>
<td>Medasso</td>
<td>2 y</td>
<td>mar 2018</td>
</tr>
<tr>
<td><strong>BE Consensus</strong></td>
<td>2 y</td>
<td><strong>oct 2018</strong></td>
</tr>
<tr>
<td>Handouts ITM</td>
<td></td>
<td>continu</td>
</tr>
<tr>
<td>Website ITM Doctors</td>
<td></td>
<td>2017</td>
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<tr>
<td>Website ITM patients</td>
<td></td>
<td>2017</td>
</tr>
</tbody>
</table>

1 presentation dedicated on consensus 2017
The End

NEXT CONSENSUSMEETING 2017
‘Short version’

TRAVEL MEDICINE SEMINAR

OCTOBER 2017

Military HOSPITAL QAMH Brussels