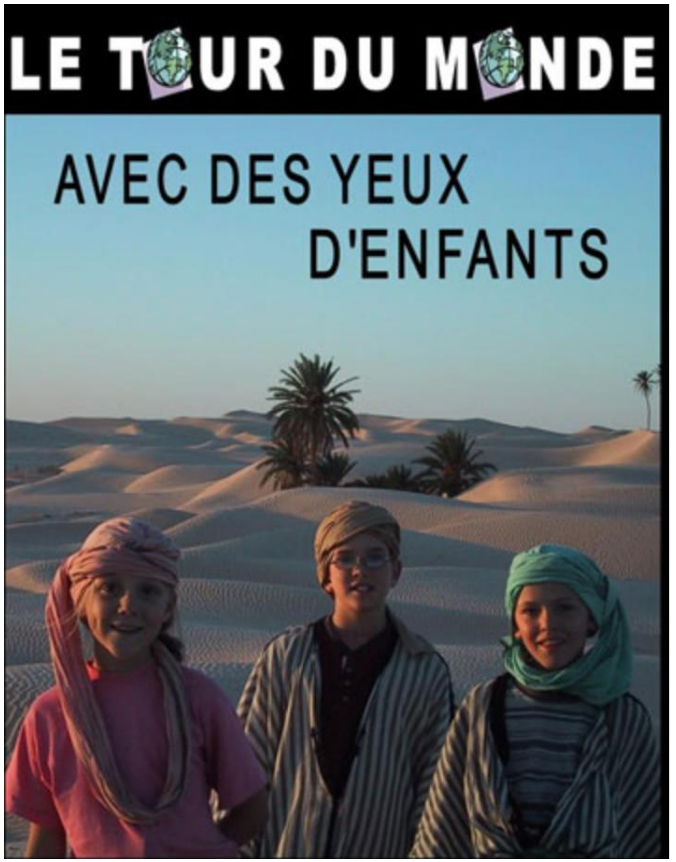
The Young Traveller

Julie Frère & Dimitri Van der Linden

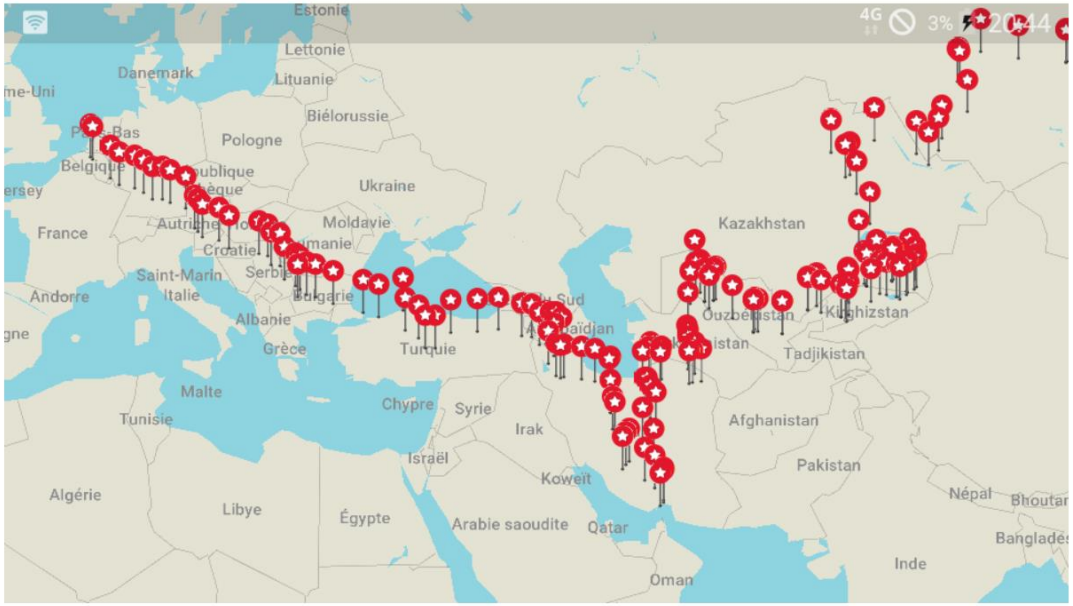
12th National Seminar on Travel Medicine – Brussels 2018


PRÉPARATIFS
TOUR DU MONDE
EN FAMILLE

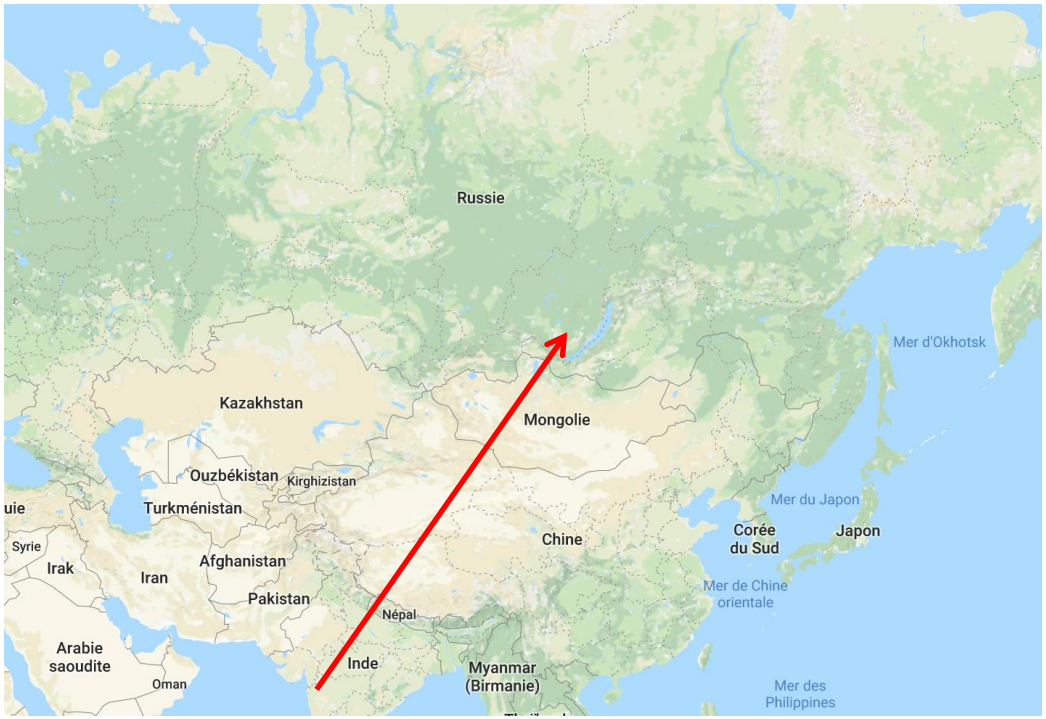

OH MY NEWS

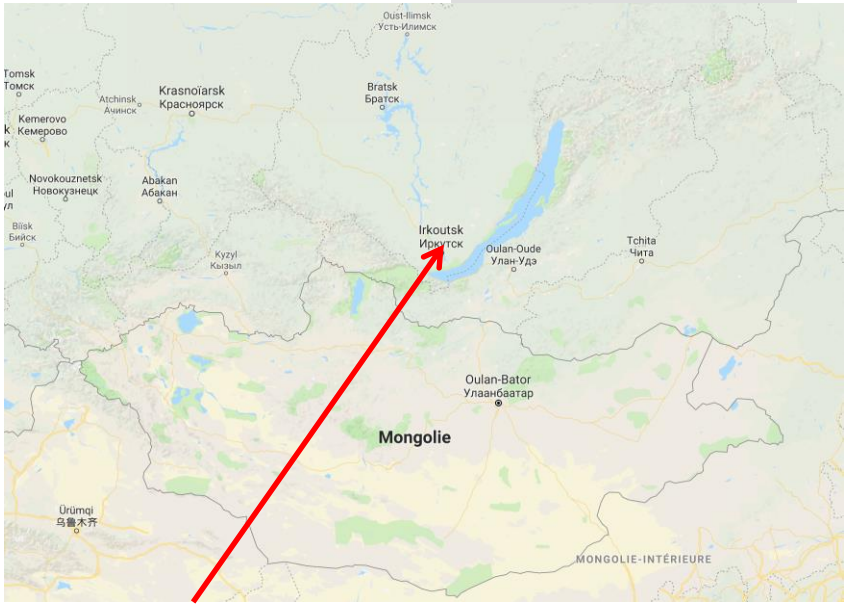

LE TOUR DU MONDE
AVEC DES YEUX
D'ENFANTS


Six Globe Truckers
Voyage Bruxelles-Sydney en camion

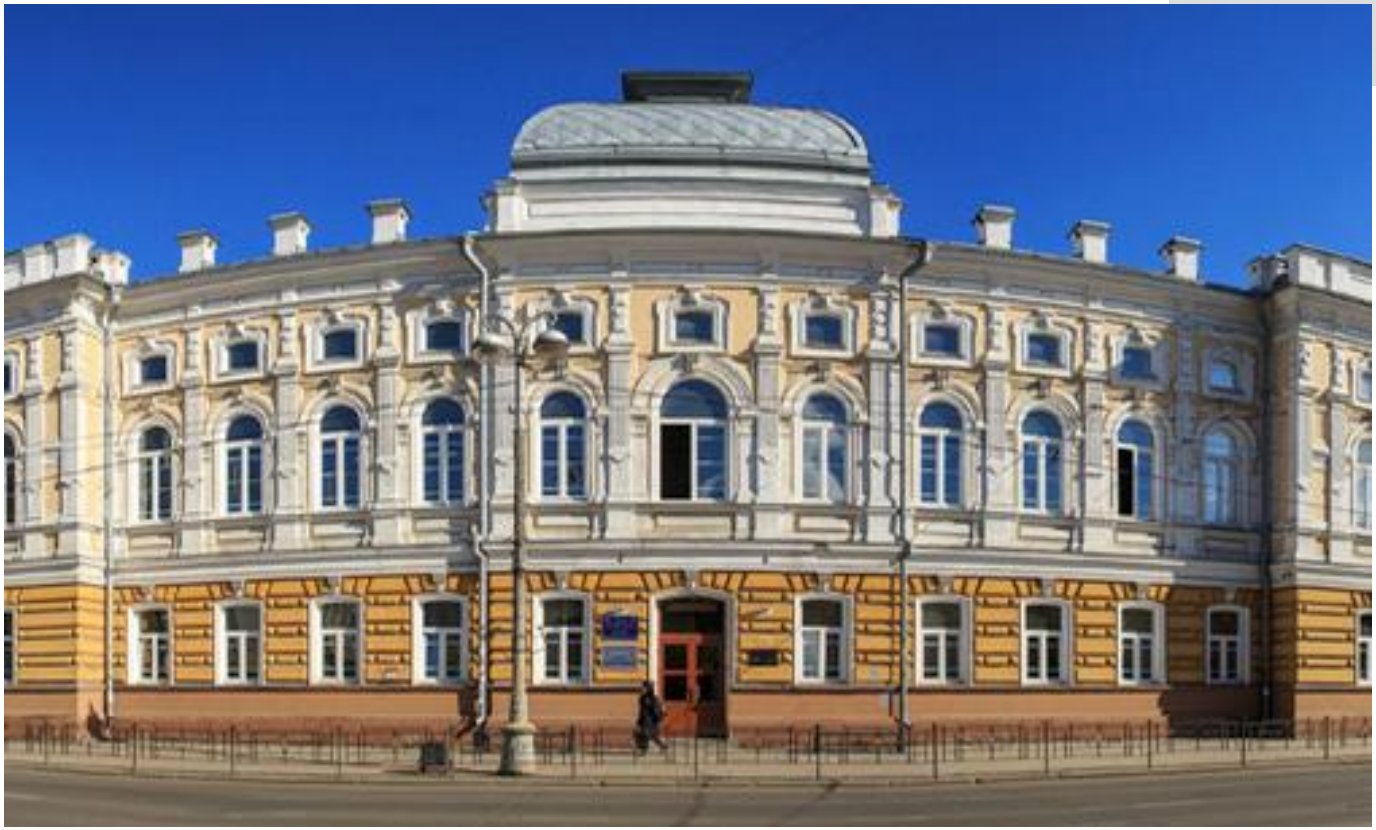

Estonie
Lettonie
Danemark
Lituanie
Biélorussie
Pologne
Belgique
Ukraine
France
Moldavie
Kazakhstan
Croatie
Saint-Marin
Italie
Andorre
Albanie
Grèce
Turquie
Malte
Tunisie
Chypre
Syrie
Irak
Israël
Koweït
Afghanistan
Pakistan
Algérie
Libye
Égypte
Arabie saoudite
Qatar
Oman
Tadjikistan
Kirghizstan
Népal
Inde

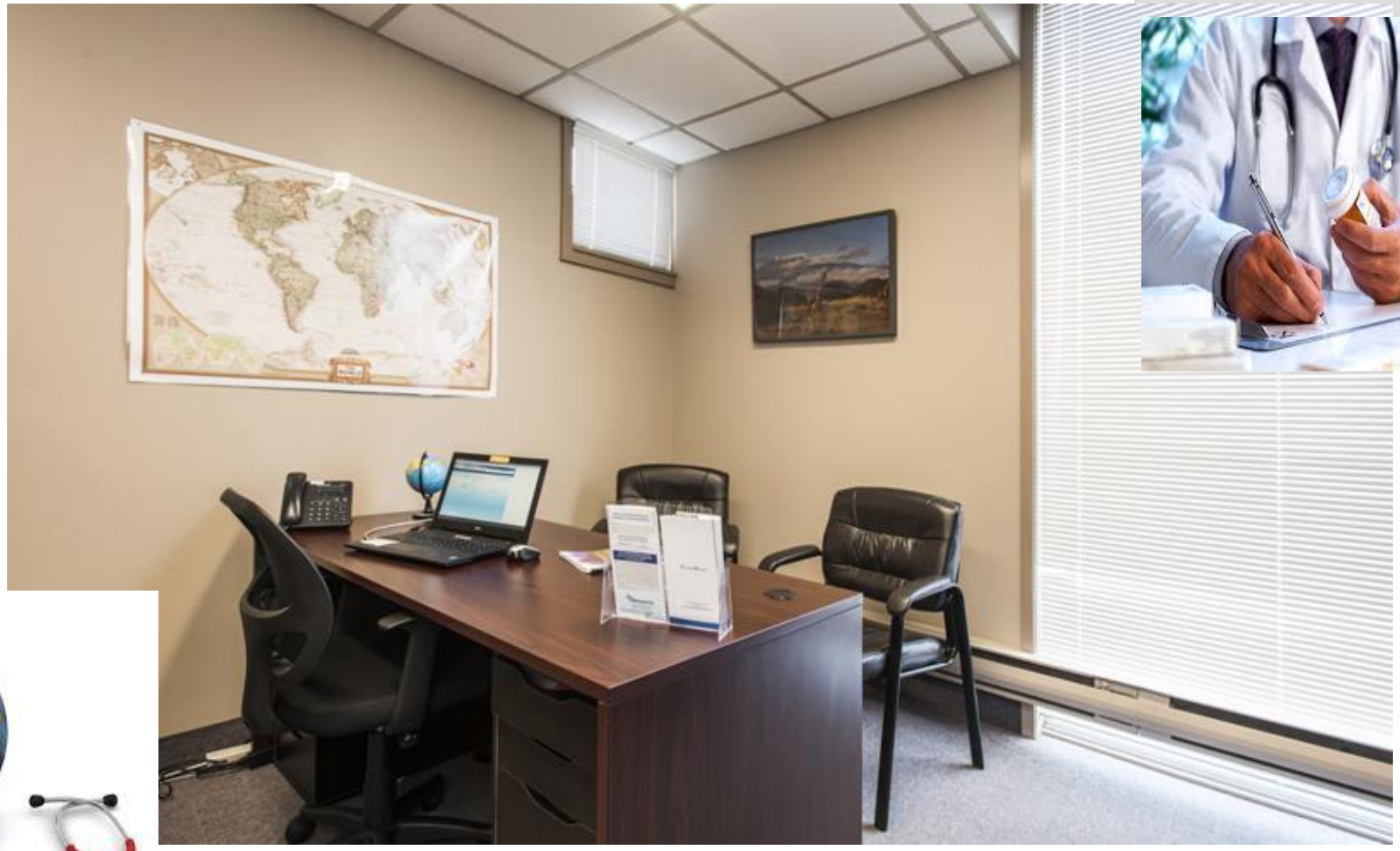
Irkoutsk, Siberia





IRKUTSK STATE UNIVERSITY





Clinical case 1 :

Adam is working for a NGO that promotes sustainable agriculture development and trade. He is planning a 2-year work placement in Vietnam.

He and is family will shortly be moving to Vietnam for two years. He has two kids of 4 and 1 year of age. They will be staying in a house in a rural area.

Both kids are up to date in their vaccinations according to the belgian schedule.

Caracteristics of travel

- Long stay
- In rural area
- Contacts with local - living

Vaccine preventable diseases in the area

- Immunization routine schedule included

- Immunizations related to travel
  - Hepatitis A
  - Japanese encephalitis
  - Typhoid fever
  - Rabies

Father's questions…

Hepatitis A

- Can both children be vaccinated?
- Are there booster doses?
- What are the risks of being infected?

Hepatitis A vaccine can be administered from 9 months of life

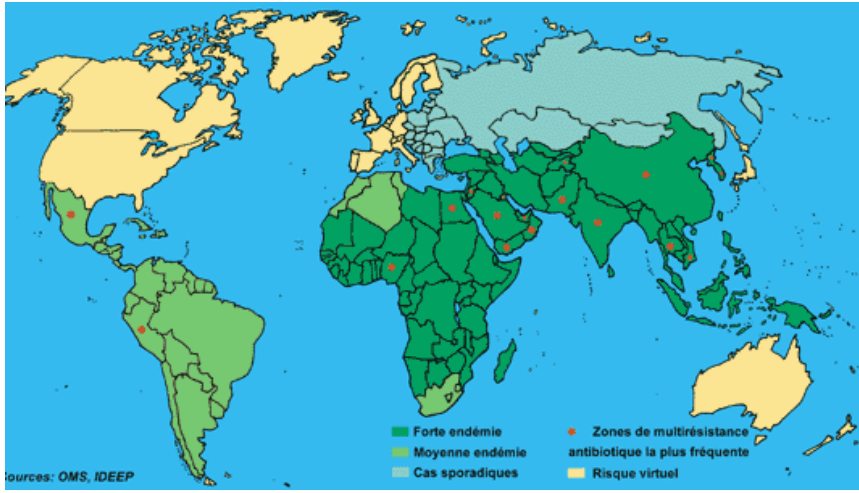
Schedule is : 2 doses administered at 6 to 12 months appart

If dose administered before 1-year of age consider adding one dose

Risk of infection is about 12.5/100000 travellers, per months of travel.

Cases are mainly observed among VFR and expatriates

Father's questions…



Typhoid fever

- Why immunization? What are the risks?
- Can both children be vaccinated?
  - What are the measures to avoid infection?
- How many doses to be protected? Booster needed?

- Vaccine recommended for travelling in high endemic regions, mainly for VFR, « Back-packers », sickle cell anemia, long stay (>3 weeks)

- **Polysaccharides vaccine : Typhym Vi (Sanofi Pasteur)**
  - Age: >2 years
  - Protective antibody : 10-14 days
  - Vaccine schedule : 1 IM dose
  - 3 weeks previous to departure a
  - ! Efficacy: 60-70% for up to 3 years, booster needed if remaining in endemic region

Father's questions…

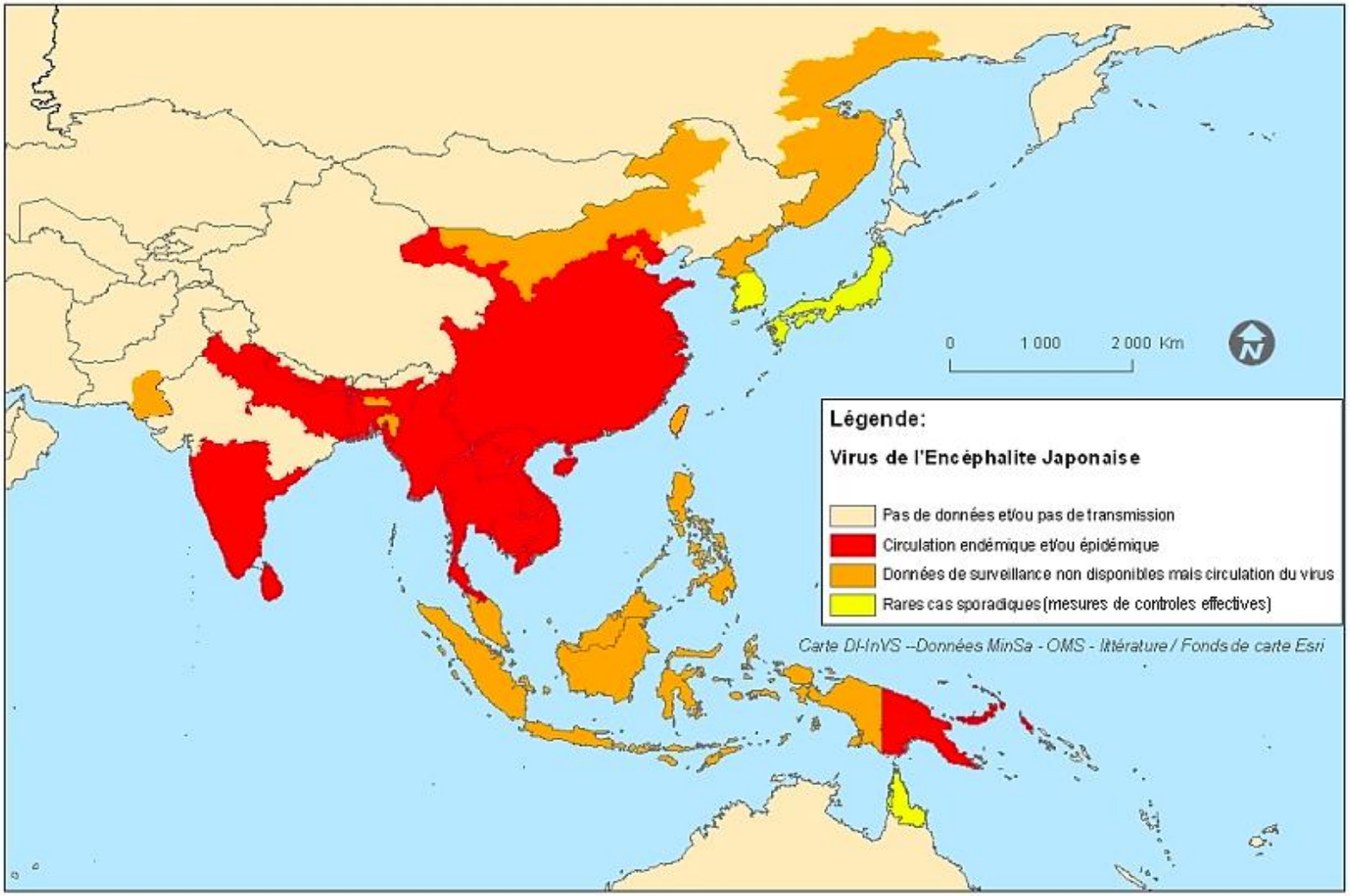
Japanese encephalitis

- Why immunization? What are the risks?
- How many doses to be protected?
- Booster needed?

Viral encephalitis transmitted through mosquitoes bites.
Incidence in travellers :

- < 1case / 1.10^6 "4-week time travellers"
- risk can increase up to 1 case /5000 "4-week time travellers", depending of destination, season, type of journey

Risk increases : long stay, rural area (reservoir)
Vietnam : All year, mainly from May to October ; especially up north


0
1 000
2 000 Km
Légende:
Virus de l'Encéphalite Japonaise
Pas de données et/ou pas de transmission
Circulation endémique et/ou épidémique
Données de surveillance non disponibles mais circulation du virus
Rares cas sporadiques (mesures de controles effectives)
Carte DI-InVS --Données MinSa - OMS - littérature / Fonds de carte Esri

Vaccine	Admin	Dosage	Age	Schedule	Boosters	Price
Ixiaro®	IM	0.5 ml	> 3 years	0-28 d	>15 m. then > 4 y if needed	83€
Ixiaro®	IM	**0.25 ml**	2 months-3 years	0-28 d	>15 m. then > 4 y if needed	83€
Ixiaro® Accelerated schedule	IM			0-8 d		

Father's questions…

Rabies

- What are the risks of exposure? Prophylactic behaviour?
- After immunization **can we** be reassured, no more risks?
- Why pre-exposure prophylaxis if cares are still necessary if bitten?
- What is the time gained thanks to PEP?

- Viral acute meningo-encephalitis. No treatment.
- Toddlers and children are at increased risks : at risk behaviour
- Pre-exposure prophylaxis can provide some protection. However, post-exposure prophylaxis remains mandatory but is simplified.
- Pre-exposure vaccination is recommended for
  - At risk groups (veterinary,…)
  - Travellers who intend to cycle or trek for long periods and in isolated areas
  - Travellers visiting isolated areas for long periods of time
  - Expatriates who settling with children
- ISP-WIV, 02/373 31 11, http://www.isp-wiv.be/odobz-domti/fr/index.html


Do not feed the monkeys in
Bali or anywhere else!

Vaccine schedule recommended

Individual	J0	J7	J28
4-year old	Japanese Enc. 1 Rabies 1	Rabies 2 Hepatitis A junior	Japanese Enc. 2 Rabies 3 Typhoid fever
1-year old	Japanese Enc. 1 Rabies 1	Rabies 2 Hepatitis A junior	Japanese Enc. 2 Rabies 3

What about BCG vaccine for us and/or for our children ?

Not routinely administered in Belgium : risk/benefit ratio

Shortage in several countries in Europe (including Belgium)

Protection in children less than 5-year old

- Depending of setting, prevalence, disease localization
- Against severe extrapulmonary forms (miliary TB and meningeal TB) 50-80%
- Efficacy waning over time

Indication for young children travelling for long periods in high endemic countries

Clinical case 3 :

Anna is a teacher and she will move to DRC with her 2 month-old daughter. She will work in a very remoted area.

Malaria physical protection

- Repellent (DEET 20-30 % max)
- Long lasting moskito-net

Repellents

Age	Nb max d'applications par jour	DEET*[1]	Picaridine	Citriodiol	IR3535[2]
6 mois-âge de la marche	1	10-30 %		20-30 %	20 %
âge de la marche-24 mois	2	10-30 %		20-30 %	20 %
24 mois-12 ans	2	20-30 %	20-30 %	20-30 %	20-35 %
> 12 ans	3	20-50 %	20-30 %	20-30 %	20-35 %

* En cas d'exposition aux anophèles vecteurs des *Plasmodium*, agents du paludisme, la concentration minimale efficace de DEET est de 30 %.

Recommandation SMV et SFP 2010

Malaria chimioprophylaxis

2 options for *P. falciparum*:

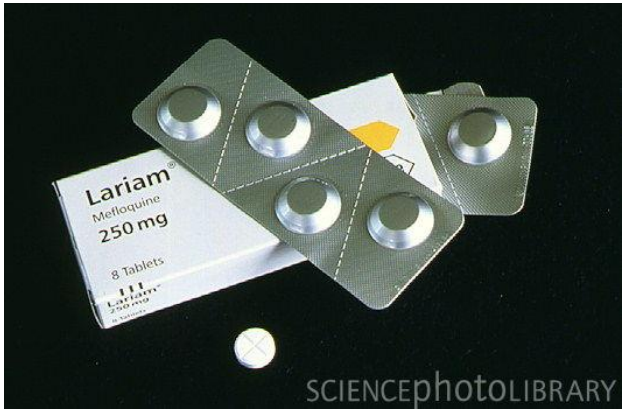
1. Mefloquine (Lariam)
2. Atovaquone-proguanil (Malarone)

NB: doxycycline not before 8 y 1.5 mg/kg/j

(max 100 mg)

Malaria chimioprophylaxis

	Lariam®
Poids (kg)	**Dose hebdomadaire en comprimés à 250 mg**
< 5	non applicable
5-10	1/8
10-20	1/4
20-30	1/2
30-45	3/4
> 45	1 (*)


Lariam®
Mefloquine
250 mg
8 Tablets
SCIENCEphotoLIBRARY


cutter
PILBOX


Jean Hervé
Produits bio & solidaires
Pâte à tartiner
CHOCOLADE
SANS HUILE DE PALME

Malaria prophylaxis yes but for how long ?

Gastro-enteritis

- 75 mmol glucose/L
- 75 mEq Na/L
- 20 mEq chlorure/L
- 10 mmol citrate/L
- Osmolarité 245 mOsm/L

DILUTE EXACTLY ACCORDING TO INSTRUCTIONS !

Gastro-enteritis

- Continue breastfeeding
- ORS: 10 ml/kg for every episode of diarrhea
- ORS: 75 ml/kg in 4h if moderate dehydration
- No imodium in young infants
- Tiorfix baby or junior : to stop if signs of dysentery
- Azithromycine if dysentery : 10 mg/kg during 3 days
  - Syrup 200 mg/5ml
  - (Max 500 mg 1x/jour)

Vaccines

How to proceed doc ??

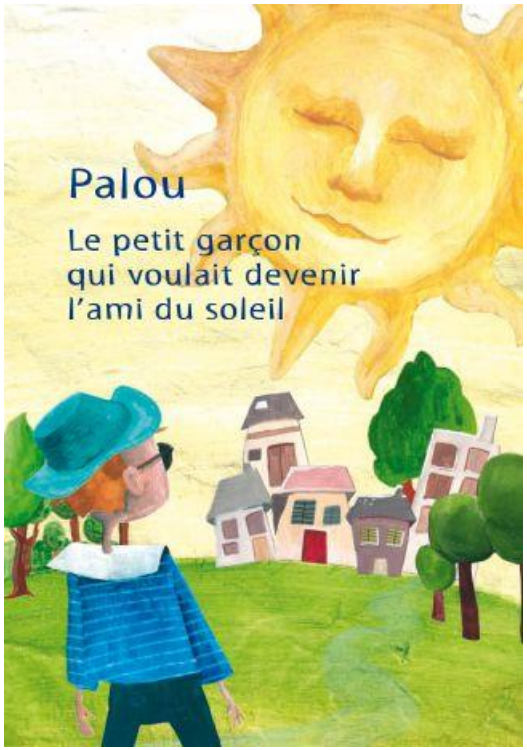
Vaccines

Vaccines

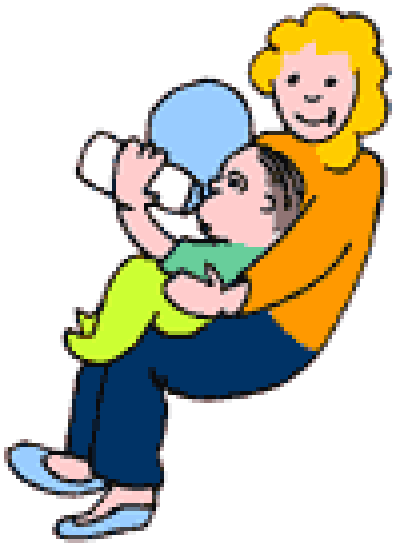
- Belgian schedule : primo-vaccination
- At 9 months : Yellow Fever + MMR
  (if possible at 1 month apart)
- At 12 months : Synflorix + MMR + Hepatitis A
- At 15 months : Hexavalent booster + Quadrivalent conjugated meningococcal vaccine
- At 2 years : Typhoid fever + 2d dose of Hepatitis A + Yellow fever vaccine (2d dose)
- + Rabies and BCG

Belgium YF guidelines - 2017

- In certain conditions, a single booster is recommended (before the next exposure, **certificate is valid 1 year**)
  - Pregnant woman
  - **Children younger than 24 month**
  - Interval of less than 28 days between YF vaccine and another live vaccine (exemple MMR)
- Testing for neutralising antibodies or booster after 10 years is necessary for people with reduced immunity :
  - Due to HIV (any CD4 count)
  - Due to immunosuppressive medication (high dose of cortisone,…)
  - Persons who received a YF vaccination before they had a bone marrow transplantation (revaccination is indicated if no CI)
- In case of high risk exposure to YF, a single booster or testing neutralising antibodies should be considered after 10 years :
  - Labo workers handling with wild YF
  - Persons working in region with YF outbreak


Palou
Le petit garçon
qui voulait devenir
l'ami du soleil


AIRBUS A380
A380



Fir skills


europ
assistance

Thank you

Questions… Comments…

International/National travel vaccination guidelines/advices

International Travel guidelines:

- WHO: The Green Book Ch. 6
- The Yellow book 2016 (CDC health information for international travel)

National guidelines:

- Australia
- Belgium - Institute for Tropical Medicine

Recent supportive publications:

- Travel Medicine Research Priorities: Establishing an Evidence Base,
  - Elizabeth A. Talbot et al. Journal of Travel Medicine 2010; Volume 17 (Issue 6): 410–415
- GeoSentinel Surveillance of Illness in Returned Travellers, 2007–2011,
  - Karin Leder et al, Annals of Internal Medicine, 2013, Volume 158; Number 6: 456-68

Vaccines' prices

Maladie visée	Vaccin	Prix / dose	Nb doses/vaccination complète	Prix du schéma total
Polio (booster)	Imovax Polio (SPMSD)	9,65€	/	/
Meningo ACWY	Nimenrix (GSK)	52,60€	1-3 (selon âge)	52,6€-157,8€
	Menveo (Novartis)	52,60€	1 (après 2A)	52,6€
Yellow fever	Stamaril (SPMSD)	15,31€	1	/
Typhoid fever	Typhérix (GSK)	24,07€	1/3ans	/
	Typhim Vi (SPMSD)	26,02€	1/3ans	/
Hepatitis A	Havrix (Jr) (GSK)	45,66€(30,04€)	2	60,08€
	Vaqta (Jr) (SPMSD)	51,43€(33,68€)	2	67,36€
Tick-born encephalitis	FSME Immun (Jr)	39,73€(39,17€)	3 – 4 (accéléré)	117,51 – 156,68€
Japanese encephalitis	Ixiaro	83,28€	3	249,84€
Rabies	Rabipur/Vaccin rabique Merieux	39,19€	3	117,57€

Vaccines for international travel

All inactivated vaccines

Yellow fever : see map, patient's situation,

HIV : see CD4 count > 200 or children 9 months-5 years with >15% CD4

Yellow fever vaccine

- 19 SOT recipients = vaccine given inadvertently
  - Nonserious side effects reported

- Experience from Brazil
  - Publications pending

Azevedo et al. Transpl Infect Dis 2012; 14:237-241

Malaria non compliquée + green flags

- Parasitémie <1-2% ou < 100.000 trophozoïtes/µL
- Bilirubine < 1.3 mg/dl
- Absence de signe de diathèse hémorragique
- Enfant en bon état général, qui ne vomit pas et >1 an
- Pas de prise de malarone en prophylaxie
- Médicament PO disponible et donné au patient ou parents en mains propres, avant son retour à domicile, prise de la première dose devant vous, pas de vomissement.
- Parents fiables et follow-up étroit

→ Prise en charge ambulatoire

Traitement malaria pédiatrique

Artemisinine

- Composé actif principal : Artemisia annua (Asie)
- Plusieurs dérivés:
  - **Artesunate** : esther hydro-soluble iv, im, ir (po)
  - Artemether : absorption variable, im, liposoluble
- Avantages:
  - Délai action **rapide**
  - Actif sur tous types de Plasmodium
  - Facilité d'administration
  - **Peu effets 2nd** (pas hypoglycémie)

Traitement malaria pédiatrique

1. Malaria non-compliquée

- **MALARONE®** (Atovaquone-Proguanil) : 3 jours de traitement

Voir tableau pour doses

- **QUININE** PO 10 mg/kg 5 jours (ou 3 à 7 jours en association avec clinda)
- **RIAMET®** (20 mg d'artéméther et de 120 mg de luméfantrine)
  - À partir de 12 ans et 35 kg
- **EURARTESIM®** (pipéraquine tétraphosphate/dihydroartémisinine) 3 jours

Voir tableau pour doses

Traitement Malaria : doses pédiatriques

Molécule	Dose
Atavaquone-proguanil (Malarone°) Dose quotidienne À prendre durant 3 jours consécutif Pas recommandé si ppx par Atovaquone-proguanil Pas recommandé si insuffisance rénale (ClCr<30ml/min)	5-8kg : 2 comprimé pédiatrique 1x/j
	9-10 kg : 3 comprimé pédiatrique 1x/j
	11-20 kg : 1 comprimé adulte 1x/j
	21-30 kg : 2 comprimés adulte 1x/j
	31-40 kg : 3 comprimés adulte 1x/j
	>40 Kg : 4 comprimé adulte 1x/j
Arthemeter-Lumefantrine (Riamet°) 3 jours de traitement, total de 6 doses H0, H8, H24, H36, H48, H60 Pas recommandé si ppx par Lariam Pas recommandé chez <5kg, femme enceinte	5-<15 kg : 1 comprimé/dose
	15-<25 kg : 2 comprimés/dose
	25-<35 kg : 3 comprimés/dose
	>35 kg : 4 comprimés/dose

Medasso 2013 – CDC Yellow book 2018

Traitement malaria pédiatrique

EURARTESIM®

Poids corporel (kg)	Dose quotidienne (mg)		Posologie (Dosage du comprimé et nombre de comprimés par prise)
	Pipéraquine (PQP)	Dihydroartemisinine (DHA)	
5 à < 7	80	10	½ comprimé à 160/20 mg
7 à < 13	160	20	1 comprimé à 160/20 mg
13 à < 24	320	40	1 comprimé à 320 mg/40 mg
24 à < 36	640	80	2 comprimés à 320 mg/40 mg
36 à < 75	960	120	3 comprimés à 320 mg/40 mg
75 à 100	1 280	160	4 comprimés à 320 mg/40 mg
> 100	Il n'existe pas de données permettant d'établir la posologie adaptée chez les patients pesant plus de 100 kg.		

Traitement malaria pédiatrique

2. Malaria compliquée

- **QUININE** (quinine dihydrochloride Sterop, amp 250mg/2ml)

Dose de charge 20mg/kg (max 1,2g) dans 10 cc/kg de G5% en 4h, puis 10mg/kg dans 10 cc/kg G5% en 4h, toutes les 8h

Associer le lendemain CLINDAMYCINE 5 mg/kg/6h pendant 5 jours

- **MALACEF®** (Artésunate IV) 2,4 mg/kg à 0 h, 12 h et 24 h, puis toutes les 24 h pendant 3 jours

Revised dose recommendation for parenteral artesunate in young children with severe malaria

Children weighing less than 20 kg should receive a higher parenteral dose of artesunate (3 mg/kg/dose) than larger children and adults (2.4 mg/kg/dose) to ensure equivalent drug exposure.
Strong recommendation based on pharmacokinetic modelling

The dosing subgroup reviewed all available pharmacokinetic data on artesunate and the main biologically active metabolite dihydroartemisinin following administration of artesunate in severe malaria (published pharmacokinetic studies from 71 adults and 265 children). Simulations of artesunate and dihydroartemisinin exposures were conducted for each age group. These showed underexposure in younger children. The revised parenteral dose regimens are predicted to provide equivalent artesunate and dihydroartemisinin exposures across all age groups.

Other considerations

Individual parenteral artesunate doses between 1.75 and 4 mg/kg have been studied and no toxicity has been observed. The GRC concluded that the predicted benefits of improved antimalarial exposure in children are not at the expense of increased risk.

Hendriksen IC, Mtove G, Kent A, Gesase S, Reyburn H, Lemnge MM, et al. Population pharmacokinetics of intramuscular artesunate in African children with severe malaria: implications for a practical dosing regimen. Clin Pharmacol Ther 2013;93:443–50.

Zaloumis SG, Tarning J, Krishna S, Price RN, White NJ, Davis TM, McCaw JM, Olliaro P, Maude RJ, Kremsner P, Dondorp A, Gomes M, Barnes K, Simpson JA. Population pharmacokinetics of intravenous artesunate: a pooled analysis of individual data from patients with severe malaria. CPT Pharmacometrics Syst Pharmacol. 2014;3:e145.

Artesunate versus quinine for treating severe malaria (Review)

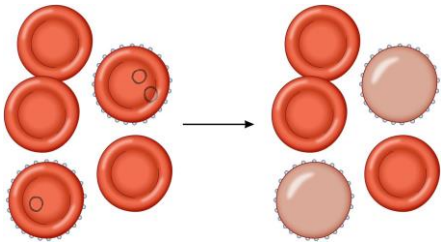
Sinclair D, Donegan S, Isba R, Lalloo DG

Artesunate should be the drug of choice for treating severe malaria in adults and children

Delayed haemolysis after artesunate treatment…

Delayed haemolysis (starting >1 week post-treatment)

- In hyperparasitemic patients
  - In young children
  - In returning travellers



Rapid killing of ring-stage parasites

Which are taken out from red blood cells by the spleen

Red cells return to circulation with reduced life-span

Predictable event!!

Hyperparasitemic patients must be followed-up carefully!!

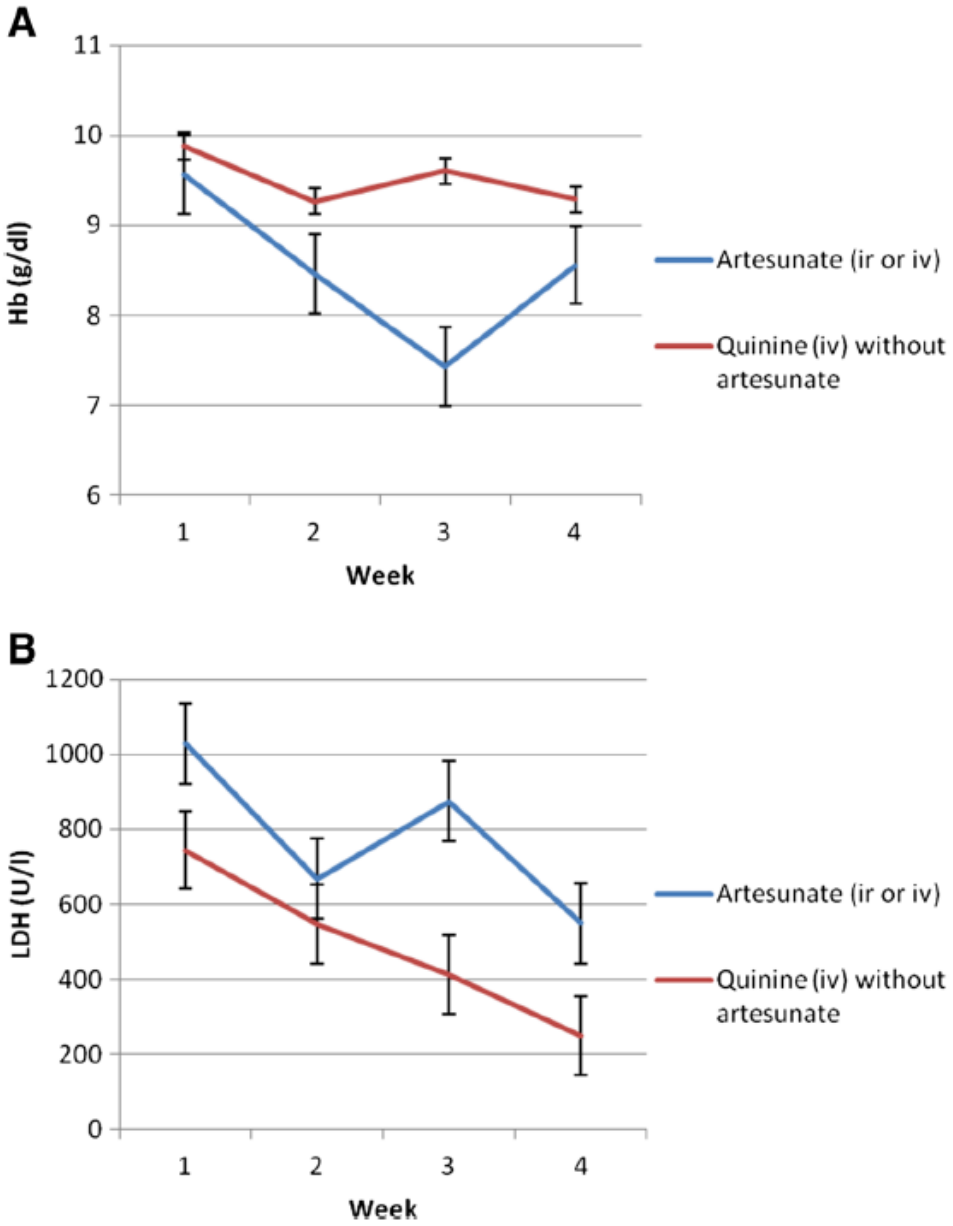


Figure 1 Time course of median weekly Hb (A) and LDH (B) in patients treated with artesunate (n = 8) and in patients treated with quinine (n = 8). ir: intrarectal; iv: intravenous. Mean ± standard error of the mean is displayed.

Case Report

Severe delayed haemolytic anaemia associated with artemether-lumefantrine treatment of malaria in a Japanese traveller☆

Chihiro Hasegawa [a], Masaharu Kudo [b], Haruhiko Maruyama [c], Mikio Kimura [d, *]

[a] *Department of Infectious Diseases, Nagoya City East Medical Centre, Nagoya, Japan*
[b] *Department of Pharmacy, Nagoya City East Medical Centre, Nagoya, Japan*
[c] *Division of Parasitology, Department of Infectious Diseases, Faculty of Medicine, University of Miyazaki, Miyazaki, Japan*
[d] *Department of Internal Medicine, Shin-Yamanote Hospital, Japan Anti-Tuberculosis Association, Tokyo, Japan*

References

International/National travel vaccination guidelines/advices

International Travel guidelines:

- WHO: The Green Book Ch. 6
- The Yellow book 2016 (CDC health information for international travel)

National guidelines:

- Belgium - Institute for Tropical Medicine – Antwerpen

Itg.be

Recent supportive publications:

- Travel Medicine Research Priorities: Establishing an Evidence Base,

  Elizabeth A. Talbot et al. Journal of Travel Medicine 2010; Volume 17 (Issue 6): 410–415

- GeoSentinel Surveillance of Illness in Returned Travellers, 2007–2011,

  Karin Leder et al, Annals of Internal Medicine, 2013, Volume 158; Number 6: 456-68

Malaria prévention médicamenteuse

	Nivaquine®
Poids (kg)	**Dose hebdomadaire en comprimés de 100 mg**
5-6	¼
7-10	½
11-14	¾
15-18	1
19-24	1,25
25-35	2
36-50	2,5
> 50	3

Zone A : 5 mg/kg/semaine

Altitude

< 2 year : not above 2000 m
< 10 years : not above 3000 m

http://www.itg.be/ITG/Uploads/MedServ/faltitude.pdf