Fever after a stay in the Tropics

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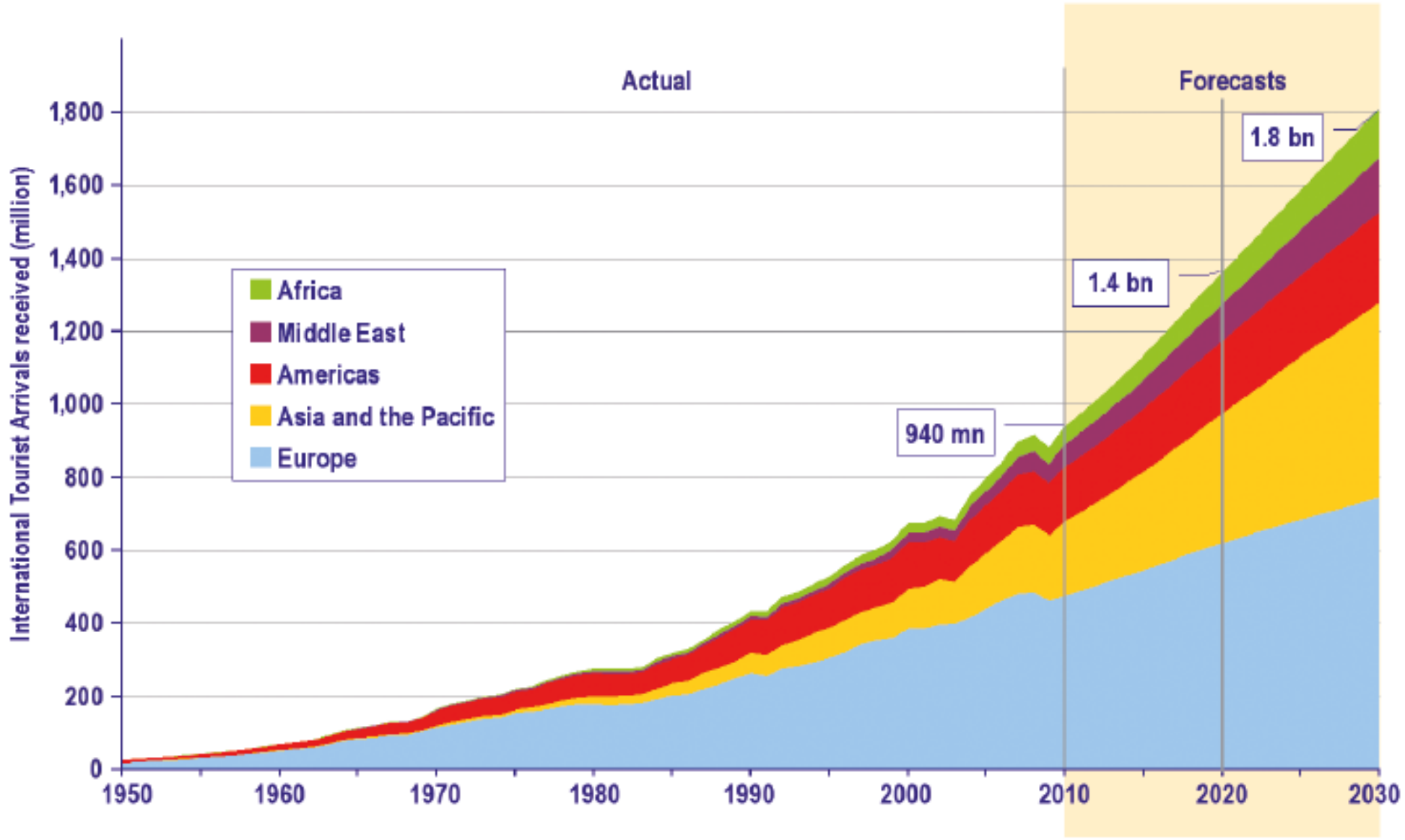
Madrid, 07 June 2017

Outline

- Introduction
- Epidemiology of travel-related fever
- Update in the management of the main imported tropical conditions

UNWTO Tourism Towards 2030: Actual trend and forecast 1950-2030



Health problems in travelers “to the tropics”

- 15-65% experience some sickness
- 5-15% need to seek medical care
- 5-10% develop fever

Steffen et al. *J Infect Dis* 1987; **Hill.** *J Travel Med* 2000; **Cabada et al**. *Travel Med Infect Dis* 2009

Fever and travel: GeoSentinels studies

1996-2004

- 30 travel clinics
- 17,353 ill travelers

22.6% of consultations

Freedman et al. *N Engl J Med* 2006

2007-2011

- 53 travel clinics
- 42,173 ill travelers

23.3% of consultations

Leder K et al. *Ann Intern Med* 2013

Fever and travel

Differential diagnosis of imported fever

Table 52.2 Causes of fever by usual incubation periods and geographic distribution

Disease/organism	Distribution
Incubation <2 weeks	
Undifferentiated fever	
Malaria	Tropics, subtropics, especially Africa
Dengue	Topics, subtropics, especially Asia
Rickettsial infections	
Spotted fever rickettsiae	Widespread; species vary by region
Typhus group rickettsiae	All continents
Scrub typhus	Especially Asia
Leptospirosis	Global; more common in tropics
Typhoid and paratyphoid	Global; high risk in Indian subcontinent
Brucellosis	Widespread; more common in developing areas
Acute HIV	Global
Tularemia	Especially N America and Europe
Relapsing fever	
(tick-borne)	Widespread
(louse-borne)	Limited foci
Fever and hemorrhage	
Meningococcemia, leptospirosis, and other acute bacterial infections	
Dengue (see above)	
Lassa fever	Africa, especially western, sub-Saharan
Yellow fever	Sub-Saharan Africa and tropical Latin America
Hemorrhagic fever with renal syndrome	Primarily Asia and Europe
Crimean-Congo hemorrhagic fever	Africa, eastern Europe and western Asia
Other hemorrhagic fevers in Africa:	
Ebola, Marburg, Rift Valley fever	
Hemorrhagic fevers from South America caused by Junin, Machupo, Sabia, Guanarito viruses	
Fever and CNS findings	
Meningococcal meningitis and many bacteria, viruses, and fungi with wide distribution	
African trypanosomiasis (sleeping sickness)	Focal areas of sub-Saharan Africa
Japanese encephalitis	Primarily Asia
Tick-borne encephalitis	Central and eastern Asia; far eastern Russia, Asia
Polio	Primarily Africa, parts of Asia
West Nile encephalitis	Widespread in Africa, Europe, Asia, Americas
Rabies	Most common in parts of Africa, Asia, Latin America
Angiostrongylus cantonensis	Most common in East, SE Asia, scattered cases elsewhere
Fever and pulmonary findings	
Influenza and other respiratory viruses, pneumococcal pneumonia, mycoplasma, Chlamydia, coronavirus	
Legionnaires'	Widespread; outbreaks in hotels, in cruise ships
Acute histoplasmosis	Especially in the Americas
Acute coccidioidomycosis	Americas
Hantavirus pulmonary syndrome	Widespread, especially in the Americas
Q fever (see below)	
Melioidosis	Especially SE Asia
Incubation 2 weeks to 2 months	
Malaria, typhoid fever, leptospirosis, brucellosis, African trypanosomiasis, melioidosis, and many of the hemorrhagic fevers and fungal infections can have incubation periods that exceed 2 weeks.	
Amebic liver abscess	Most common in developing regions
Toxoplasmosis, acute	Worldwide
Hepatitis A	Most common in developing areas
Hepatitis E	Widespread; outbreaks in Asia, Africa, Latin America
Schistosomiasis (acute)	Mainly in Africa; also in Asia, Latin America
Q fever	Widespread
Bartonellosis (*B. bacilliformis*)	Especially mountain areas of South America
Incubation >2 months	
Many of these infections can have incubation period shorter than 2 months	
Malaria, amebic liver abscess, melioidosis, and rabies, listed above, can have incubation >2 months.	
Hepatitis B	Worldwide
Leishmaniasis, visceral	Areas of risk in Africa, Asia, South America, southern Europe
Tuberculosis	Worldwide with wide range in incidence rates
Filariasis, lymphatic	Tropical regions
Fascioliasis	Sheep and cattle raising areas

© Elsevier 2004. Keystone *et al.* Travel Medicine

Main causes of imported fever (%)

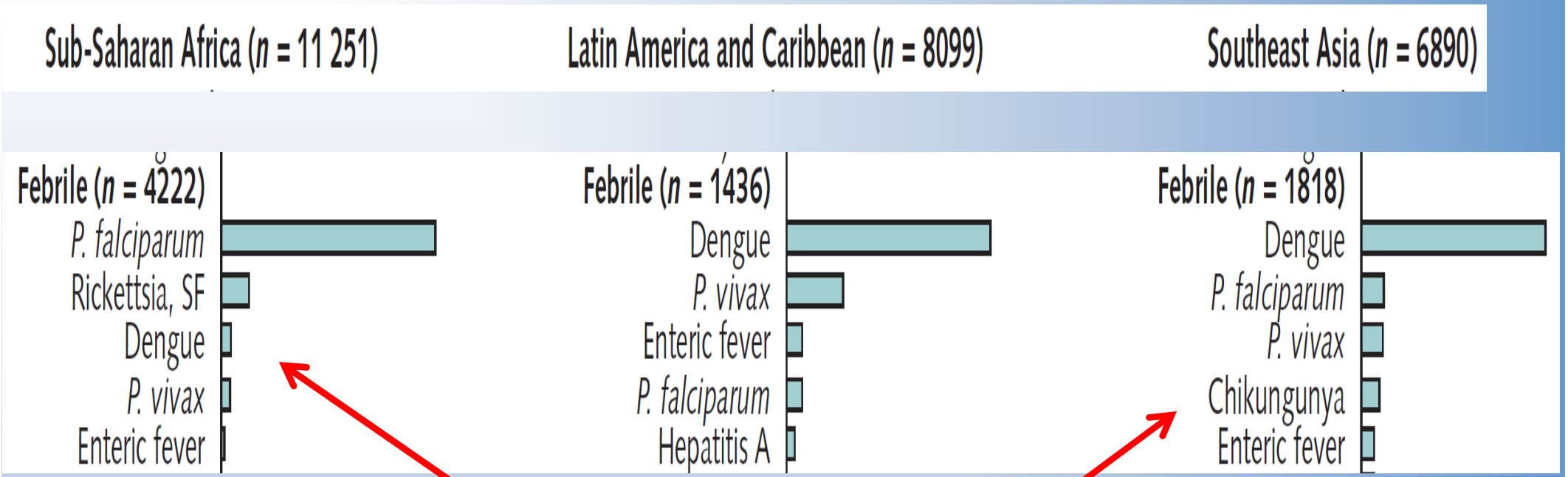
	ITMA, n=2071 Bottieau et al. *Medicine* 2007	GeoSentinel, n=6957 Wilson et al. *Clin Infect Dis* 2007
Malaria	27	21
Respiratory illness	10	14
Bacterial enteritis	6	8
Skin/soft tissue infection	4	4
Genito-urinary infection	3	4
Dengue	3	6
Enteric fever	1	2
Unknown etiology	23	22

Top tropical conditions, ITMA 2000-2006

Africa (n=1401)	Asia (n=381)	America (n=146)
P.falciparum malaria (30%)	Dengue (13%)	
Non-falc. malaria (5%)	Non-falc. malaria (9%)	Dengue (9%)
Rickettsial infection (4%)	Enteric fever (3%)	Non-falc. malaria (4%)
Katayama (2%)	*P.falciparum* malaria (2%)	Protoz. enteritis (2%)

Bottieau et al. *Arch Intern Med* 2006; *Medicine* 2007

Top tropical conditions, GeoSentinel 2007-2011



Evolving epidemiology

Leder K et al. *Ann Intern Med* 2013

Top tropical conditions, recent impact of epidemics

Chikungunya Virus and the Global Spread of a Mosquito-Borne Disease

Scott C. Weaver, Ph.D., and Marc Lecuit, M.D., Ph.D.

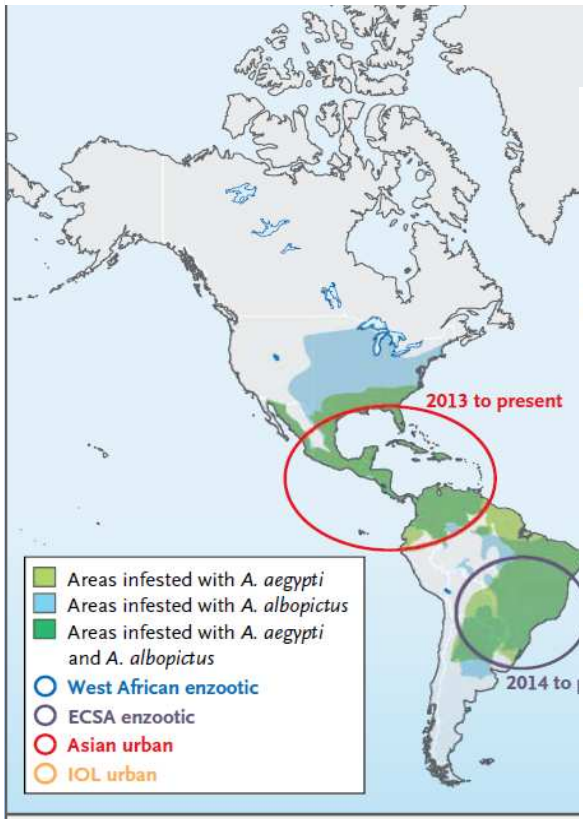


Figure 2. Origin, Spread, and Distribution of Chikungu

The map shows the African origins of enzootic chikun and Indian Ocean lineage (IOL) of the virus during epi peridomestic vectors, *Aedes aegypti* and *A. albopictus*,

The NEW ENGLAND

N Engl J Med 2015;372:1231-9.
DOI: 10.1056/NEJMra1406035

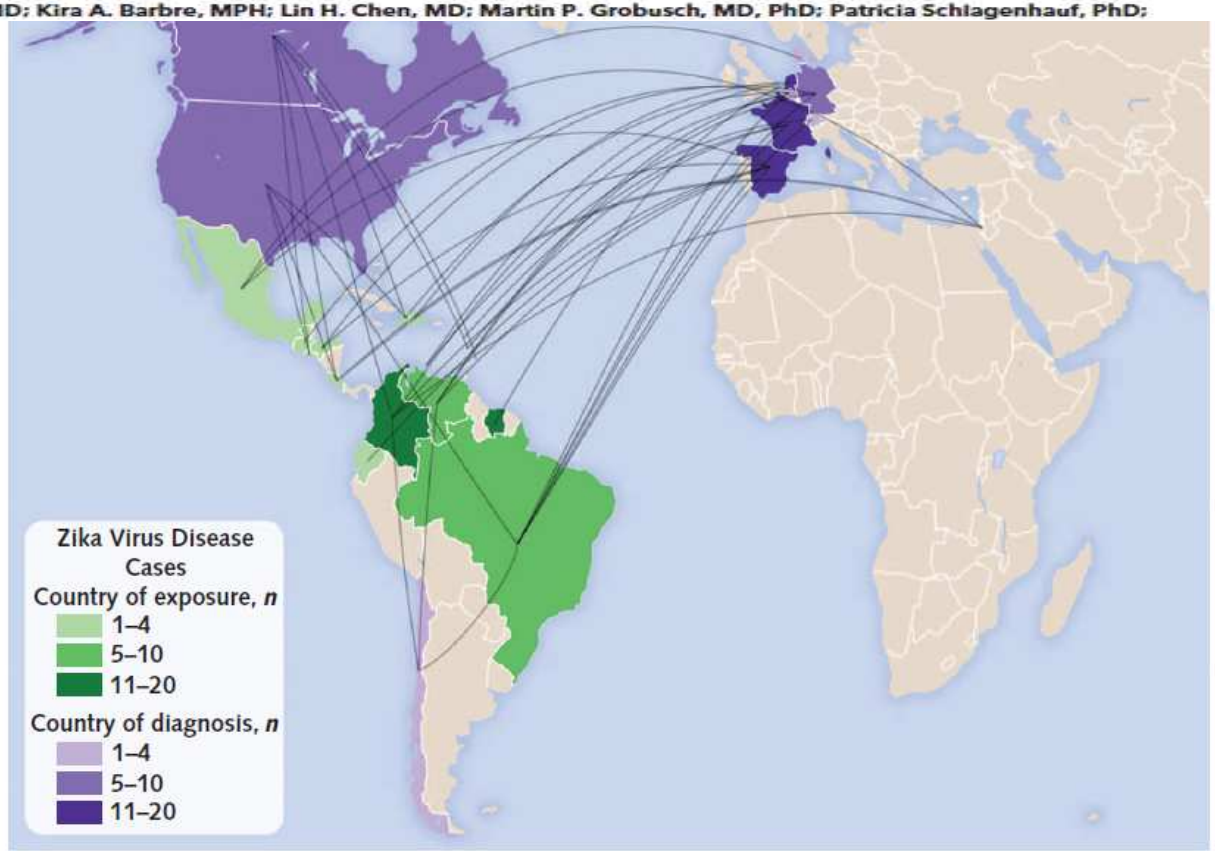
Ann Intern Med. doi:10.7326/M16-1842 www.annals.org
For author affiliations, see end of text.
This article was published at www.annals.org on 22 November 2016.

Annals of Internal Medicine ORIGINAL RESEARCH

Travel-Associated Zika Virus Disease Acquired in the Americas Through February 2016

A GeoSentinel Analysis

Davidson H. Hamer, MD; Kira A. Barbre, MPH; Lin H. Chen, MD; Martin P. Grobusch, MD, PhD; Patricia Schlagenhauf, PhD;



Tropical fever: expect … the unexpected

MAJOR ARTICLE

Acute Muscular Sarcocystosis: An International Investigation Among Ill Travelers Returning From Tioman Island, Malaysia, 2011–2012

Douglas H. Esposito,[1] August Stich,[2] Loïc Epelboin,[3,4] Denis Malvy,[5] Pauline V. Han,[1] Emmanuel Bottieau,[6]

Clinical Infectious Diseases® 2014;59(10):1401–10
Published by Oxford University Press on behalf of the Infectious Diseases Society of America 2014. This work is written by (a) US Government employee(s) and is in the public domain in the US.
DOI: 10.1093/cid/ciu622

Louseborne Relapsing Fever in Young Migrants, Sicily, Italy, July–September 2015

Alessandra Ciervo, Fabiola Mancini, Francesca di Bernardo, Anna Giammanco, Giustina Vitale, Piera Dones, Teresa Fasciana, Pasquale Quartaro, Giovanni Mazzola, Giovanni Rezza

Author affiliations: Istituto Superiore di Sanità, Rome, Italy

Emerging Infectious Diseases • www.cdc.gov/eid • Vol. 22, No. 1, January 2016

Louseborne Relapsing Fever among East African Refugees, Italy, 2015

Anna Lucchini, Filippo Lipani, Cecilia Costa, Mariaelisabetta Scarvaglieri, Rosanna Balbiano,

All patients sought care at one of the city emergency departments (EDs), reporting a 2–4-day history of fever

Emerging Infectious Diseases • www.cdc.gov/eid • Vol. 22, No. 2, February 2016

Tropical conditions (n,%) according to "latency"

	Within 1 month n=1619	During 2nd-3rd month n=228	From 4th to 12th month n=224
***P. falciparum* malaria**	401 (25)	29 (13)	10 (4.5)
Non-falciparum malaria	34 (2)	41 (18)	38 (17)
Rickettsial infection	70 (4)	-	-
Dengue	64 (4)	-	-
Katayama	28 (2)	9 (4)	1 (0.5)
Enteric fever	15 (1)	1 (0.5)	-
Amebic liver abscess	8 (0.5)	1 (0.5)	1 (0.5)
Other tropical diseases	39 (3)	4 (2)	3 (1.5)

Bottieau et al. *Arch Intern Med* 2006; *Medicine* 2007

Main diagnoses (%) according to traveler demography

	Western travelers (n=1245)	Western Expatriates (n=300)	VFR travelers (n=286)	Foreign visitors/ migrants (n=240)
***P.falciparum* malaria**	**14**	**37**	**36**	**26**
Non-falcip. malaria	**6**	**7**	**3**	**8**
Rickettsial infection	**5**	**1**	**-**	**-**
Dengue	**4**	**2**	**1**	**-**
Katayama	**3**	**1**	**-**	**-**
Bacterial enteritis	**8**	**5**	**3**	**3**
Tuberculosis	**0.25**	**0**	**3**	**9**
HIV infection, % tested	***6***	***6***	***14***	***40***

Less frequent febrile conditions, ITMA 2000-2006

- Few cases
  - *Cyclospora* enteritis (7)
  - Histoplasmosis (6)
  - Leptospirosis (6)
  - Hepatitis E (4)
  - *Cryptosporidium* enteritis (4)
  - Loeffler syndrome (3)
  - Strongyloidiasis (3)
  - Human African trypanosomiasis (3)
  - Sarcocystosis (3)
- Single cases
  - Relapsing fever
  - *I. belli* enteritis
  - Angiostrongyloidiasis

Evolution and outcome, ITMA 2000-2006

- Hospitalization : 27% (n = 564)
- Intensive care : 2% (n = 43)
- Death : 0.5% (n = 9)
  - Tropical conditions = 5 (all *P. Falciparum* malaria)
  - Cosmopolitan infections = 2
  - Non-infectious diseases = 2
  - Fever of unknown etiology = 0

Severe tropical conditions: GeoSentinel

Am. J. Trop. Med. Hyg., 88(2), 2013, pp. 397–404
doi:10.4269/ajtmh.12-0551
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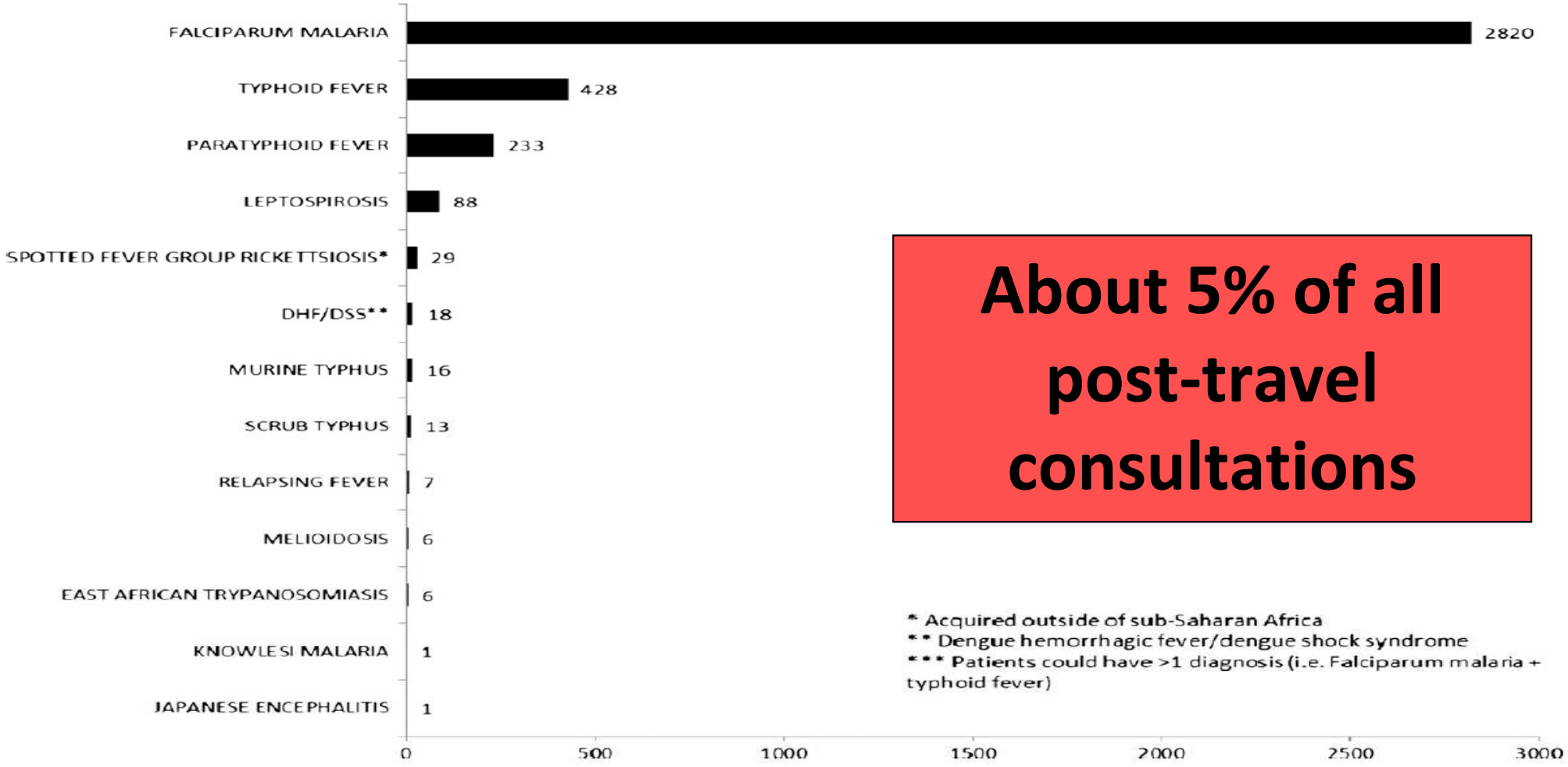
Acute and Potentially Life-Threatening Tropical Diseases in Western Travelers—A GeoSentinel Multicenter Study, 1996–2011

Mogens Jensenius,* Pauline V. Han, Patricia Schlagenhauf, Eli Schwartz, Philippe Parola, Francesco Castelli, Frank von Sonnenburg, Louis Loutan, Karin Leder, and David O. Freedman for the GeoSentinel Surveillance Network



About 5% of all post-travel consultations

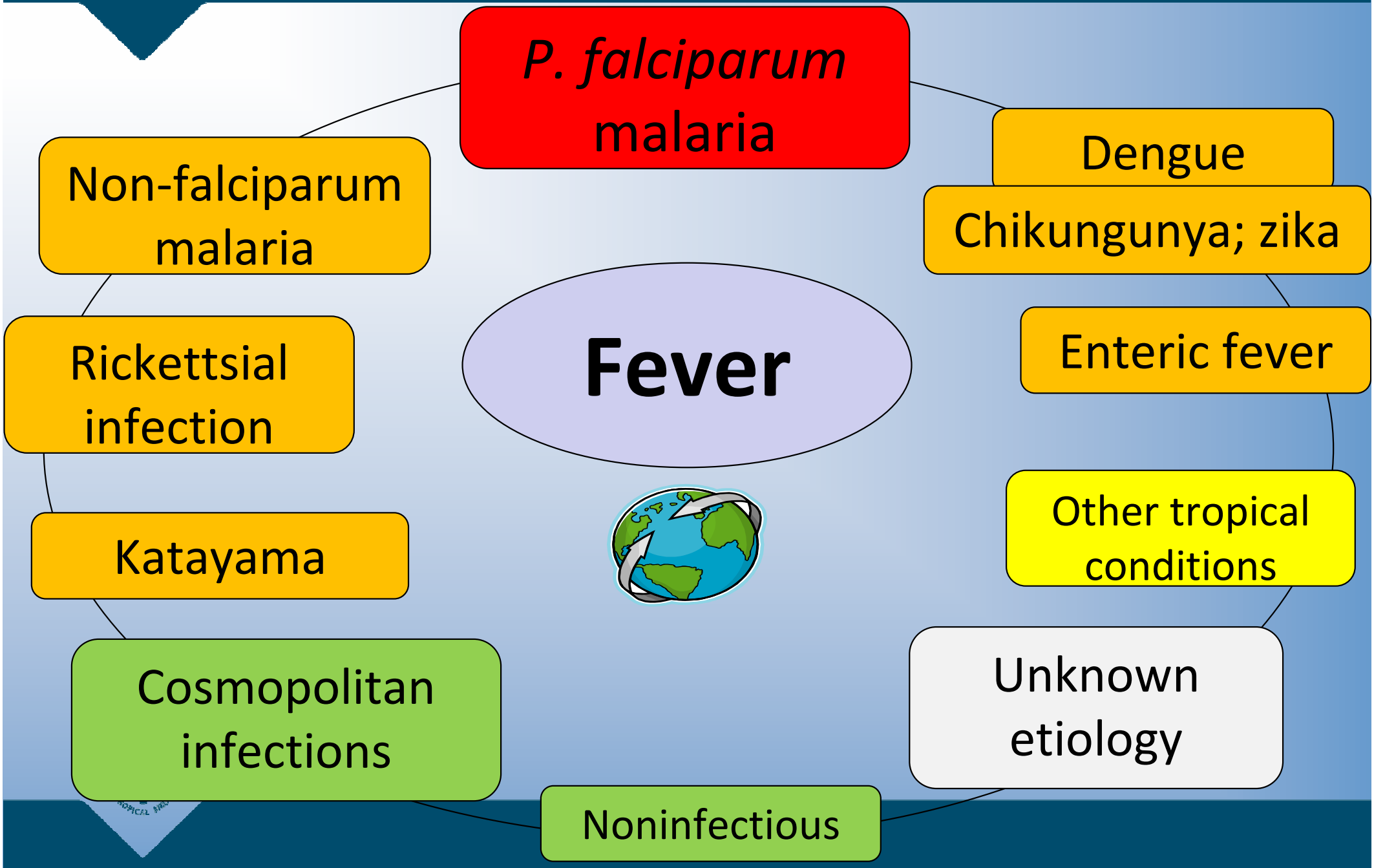
FIGURE 1. Total cases of acute and potentially life-threatening diseases ($N = 3,666$) among 82,825 ill western travelers to the tropics: data from the GeoSentinel surveillance network, 1996–2011.

Epidemiology of imported fever: conclusions

- Both tropical and cosmopolitan infections
- Etiological spectrum depending on
  - Travel destination
  - Latency period
  - Traveler demography

- Considerable morbidity
- *P. falciparum* malaria is the leading life-threatening condition

Fever and travel: diagnostic panorama



Fever and travel: recent comprehensive review

The NEW ENGLAND JOURNAL of MEDICINE

REVIEW ARTICLE

Dan L. Longo, M.D., *Editor*

Approach to Fever in the Returning Traveler

Guy E. Thwaites, F.R.C.P., and Nicholas P.J. Day, F.Med.Sci., F.R.C.P.

From the Centre for Tropical Medicine and Global Health, Nuffield Department of Medicine, University of Oxford, Oxford, United Kingdom (G.E.T., N.P.J.D.); Oxford University Clinical Research Unit, Ho Chi Minh City, Vietnam (G.E.T.); and the Mahidol–Oxford Tropical Medicine Research Unit, Faculty of Tropical Medicine, Mahidol University, Bangkok, Thailand (N.P.J.D.). Address reprint requests to Prof. Thwaites at Oxford University Clinical Research Unit, 764 Vo Van Kiet, Quan 5, Ho Chi Minh City, Vietnam, or at gthwaites@oucru.org.

N Engl J Med 2017;376:548-60.
DOI: 10.1056/NEJMra1508435

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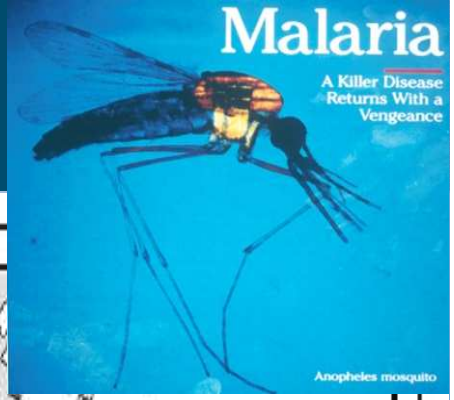
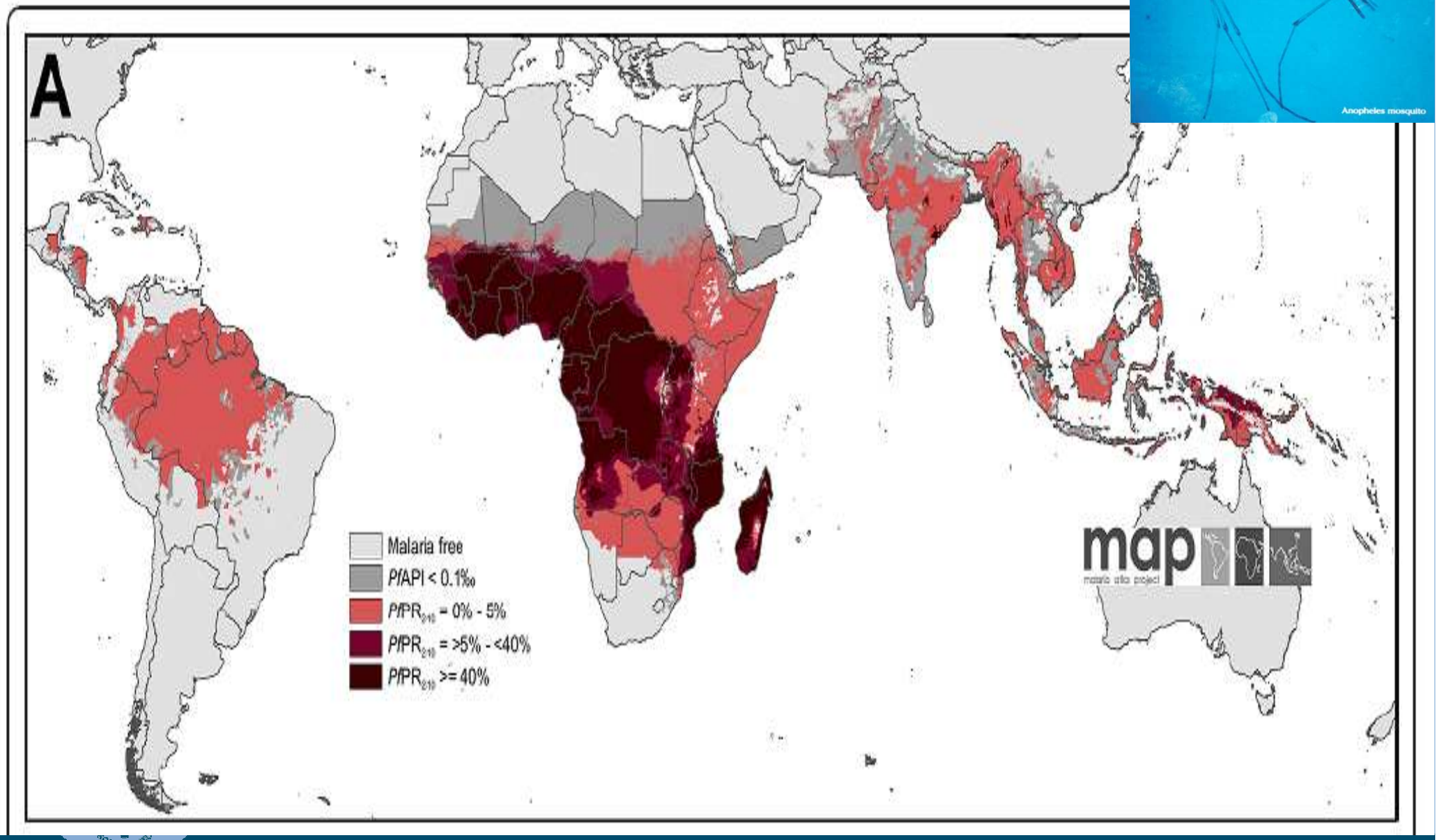
FEVER IN THE RETURNING TRAVELER IS A COMMON CLINICAL SCENARIO that often leads to hospitalization and may be the only symptom of a serious or life-threatening illness.[1] Three percent of 784 Americans who traveled abroad for short periods reported an episode of febrile illness,[2] and fever was the chief symptom in 28% of 24,920 ill travelers who presented to travel clinics on their return home.[3] The absolute number of travelers is large and rising, with the International Tourism Organization reporting 1.2 billion trips in 2015, an increase of 4.4% from the previous year.[4] The challenge presented by returning travelers with febrile illnesses is changing for two reasons. First, increasing numbers of travelers are older than 60 years of age or are seeking health care elsewhere ("medical tourists"), and these travelers are more likely than others to have clinically significant coexisting conditions and consequently increased morbidity from infections. Second, the likelihood of multidrug resistance in the infecting organisms is increasing.[5-7] The recent Ebola epidemic in West Africa, the emergence of the Middle East

Malaria





Gething et al. *Malar J* 2011

Malaria: clinical and laboratory predictors

Does This Patient Have Malaria?

Steve M. Taylor, MD, MPH
Malcolm E. Molyneux, MD, FRCP
David L. Simel, MD, MHS
Steven R. Meshnick, MD, PhD
Jonathan J. Juliano, MD, MSPH

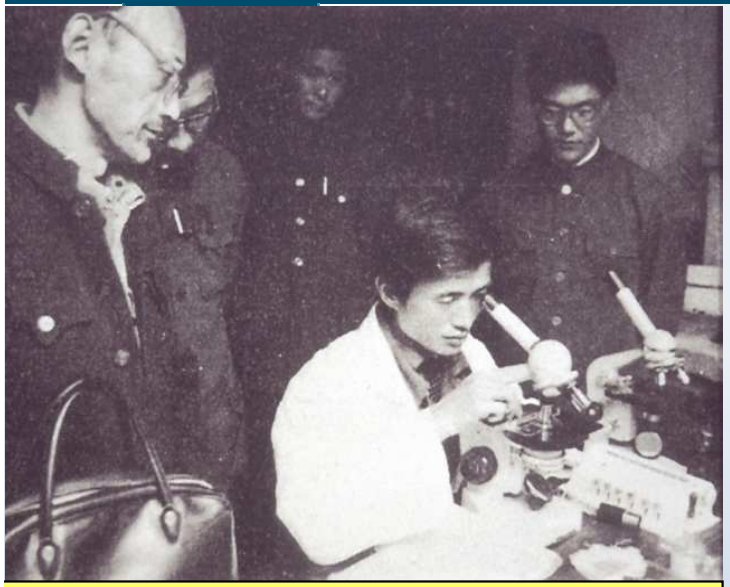
Context Malaria commonly infects residents of and travelers to tropical regions. The clinical features of infection are notoriously nonspecific but have not been comprehensively evaluated.

Objective To systematically review and synthesize data related to the predictive value of clinical findings for the diagnosis of malaria in endemic areas and in travelers returning from endemic areas.

	LR+	95% CI
• Splenomegaly	6.5	(3.9-11.0)
• *No localizing symptoms*	*4.5*	-
• Hyperbilirubinemia	7.3	(5.5-9.6)
• Thrombocytopenia	5.6	(4.1-7.5)

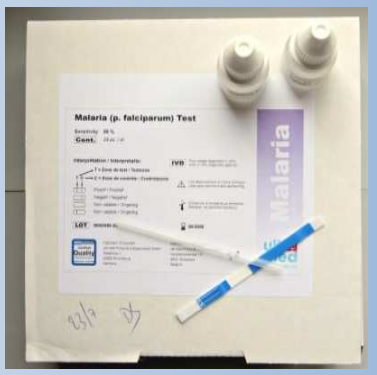
Bottieau et al. *Medicine* 2007; Taylor SM et al. *JAMA* 2010

Malaria: advances in diagnosis



Microscopy

card



dipstick

hybrid

Rapid diagnostic test (RDT)

cassette

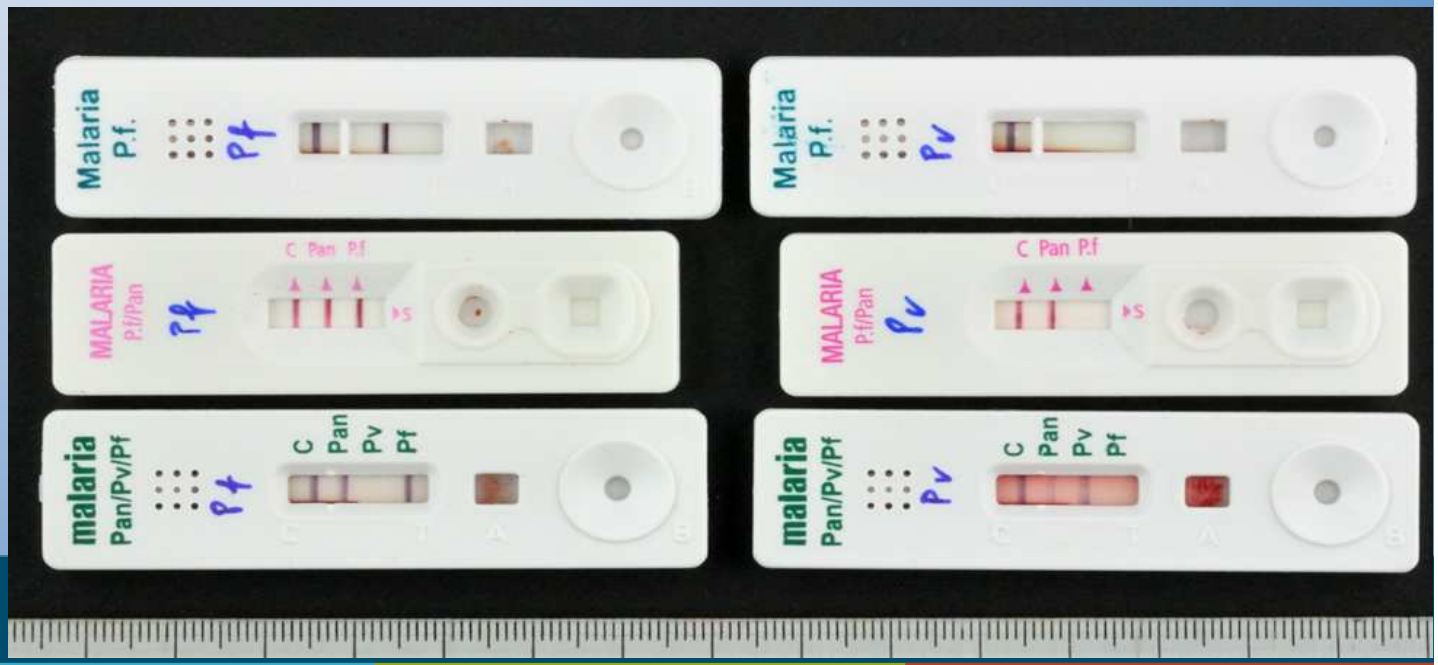
Malaria RDTs: multiple combinations

	HRP-2	pLDH	(Aldolase)
***P.falciparum*- specific**	+	+	
Pan-specific		+	+
***P.vivax*-specific**		+	

Two-band tests

Three-band tests

Four-band tests



Malaria RDTs in 2017: which one to choose?

Malaria RDTs: performance in 2017

- Accurate for diagnosis of (uncomplicated) *P. falciparum* malaria
  - Sensitivity > 95% at parasitemia > 100/µL; specificity > 95%
  - May replace microscopy in **ENDEMIC SETTINGS**
    - Abba K et al. *Cochrane Database Syst Rev* 2012
- Less accurate than EXPERT microscopy
- Equivalent to/better than ROUTINE microscopy
  - In endemic settings (Batwala *Malar J* 2010; Hendriksen *Clin Infect Dis* 2011)
  - In US hospitals (Palmer *J Clin Microbiol* 2003; Stauffer *Clin Infect Dis* 2009)

Malaria RDTs: limitations in accuracy

False negative

- Low *P. falciparum* parasitemia
- Plasmodium other than *P. falciparum*
- High *P. falciparum* parasitemia (prozone); only HRP-2
- *P. falciparum* with *pfhrp2 or 3* gene deletions; only HRP-2
- Faint test line…

False positive

- Persistence HRP-2
- Delayed reading
- Buffer substitution
- Cross reactions between species
- Concomittant conditions

Maltha J et al. *Clin Microbiol Infect* 2013

Malaria: diagnosis in travel medicine in 2017

ALWAYS perform both RDT AND microscopy

- If RDT negative and no malaria predictor, microscopy may be delayed
  - Rossi et al. *Malar J* 2012
- If RDT positive, microscopy immediately
  - Parasite load; species differentiation
- If both tests negative
  - Repeat RDT/microscopy within 12-24h especially if presence of malaria predictors (Bottieau. *Eur J Clin Microbiol Infect Dis* 2006)

Malaria management in 2017

First evaluate clinical/laboratory signs of severity

- If at least one present: **complicated (severe) malaria**

- If all absent consider outpatient treatment if
  - No co-morbidities
  - Age > 5 and < 50 years
  - No vomiting
  - Parasite load < 1%
  - (Normal bilirubinemia)

Malaria: WHO criteria of severity: for endemic settings

- Coma/convulsions
- Severe anemia
  - Hematocrite < 15%
  - Hemogl. < 5 g/dL
- Oligo-anuria < 400 ml/d
- Jaundice

- Shock
- Bleeding/DIC
- Dyspnea
- Hypoglycemia
- Parasite density > 5% of RBC

WHO. Severe malaria 2000

Severe malaria in non-endemic settings

Table 1. Clinical and biological criteria for severe malaria according to the 2000 World Health Organization definition with modifications (see * and †).

Clinical criteria
Impaired consciousness: Glasgow Coma Scale score <11*
Respiratory distress: requirement for noninvasive and/or endotracheal mechanical ventilation or spontaneous breathing with PaO_2 <60 mm Hg (if FiO_2 ≥0.21) †, and/or respiratory rate >32/min*
Multiple convulsions
Circulatory collapse: systolic blood pressure <80 mm Hg despite adequate volume repletion
Abnormal bleeding
Jaundice: clinical jaundice or bilirubin >50 µmol/L
Macroscopic hemoglobinuria: if unequivocally related to acute malaria (patients with blackwater fever were not included)
Laboratory criteria
Severe anemia: hemoglobin <5 g/dL
Hypoglycemia: blood glucose <2.2 mmol/L
Acidemia (pH<7.35) or acidosis (serum bicarbonate <15 mmol/L)
Hyperlactatemia: arterial lactate >5 mmol/L
Hyperparasitemia ≥4%
Renal impairment: serum creatinine >265 µmol/L or blood urea nitrogen >17 mmol/L*

*Coma scale criteria of 11 instead of 9; respiratory rate >32/minute and blood urea nitrogen > 17 mmol/L are modifications according to the SEAQUAMAT group [8].
†The requirement for noninvasive and/or endotracheal mechanical ventilation or spontaneous breathing with PaO_2 <60 mm Hg (if FiO_2 ≥0.21) was used specifically for this study.
doi:10.1371/journal.pone.0013236.t001

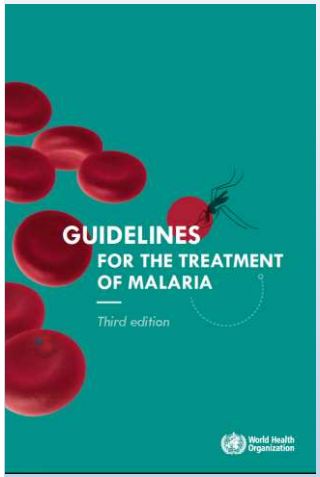
Bruneel et al. *PLoS ONE* 2010

Treatment of complicated malaria (2015, WHO)

- **First choice : IV ARTESUNATE**

  But problems of

  - availibility (no GMP-compliant product)
  - cost 60 euro per vial Malacef
  - recent evidence of toxicity (delayed hemolysis)



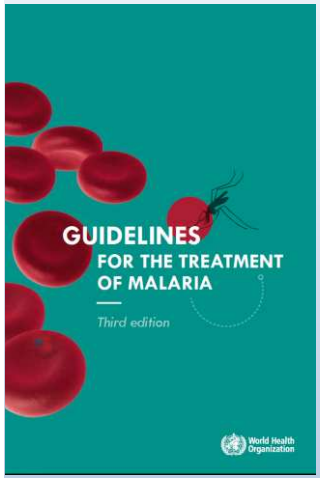
Jauréguiberry et al. *Emerg Inf Dis* 2015: prospective study: 21/78 (27%)

- Second choice: IV quinine

  But still first choice in vomiting patients or parasitemia 1-5%

Treatment of uncomplicated malaria (2015, WHO)

- *P falciparum* malaria
  - **Artemisinin-based combination treatment (ACT)**
    - Artemether/lumefantrine (Riamet)
    - Dihydroartemisinin/piperaquine (Eurartesim)
  - **Atovaquone/proguanil** (Malarone)
  - Quinine + doxycycline or clindamycine (second choice)



NB: Outpatient treatment possible in experienced centers ; (Bottieau et al. Eur J Clin Microbiol Infect Dis 2006)

- Non-falciparum malaria
  - Chloroquine or ACT (+/- primaquine for *P vivax/P ovale*)

Dengue

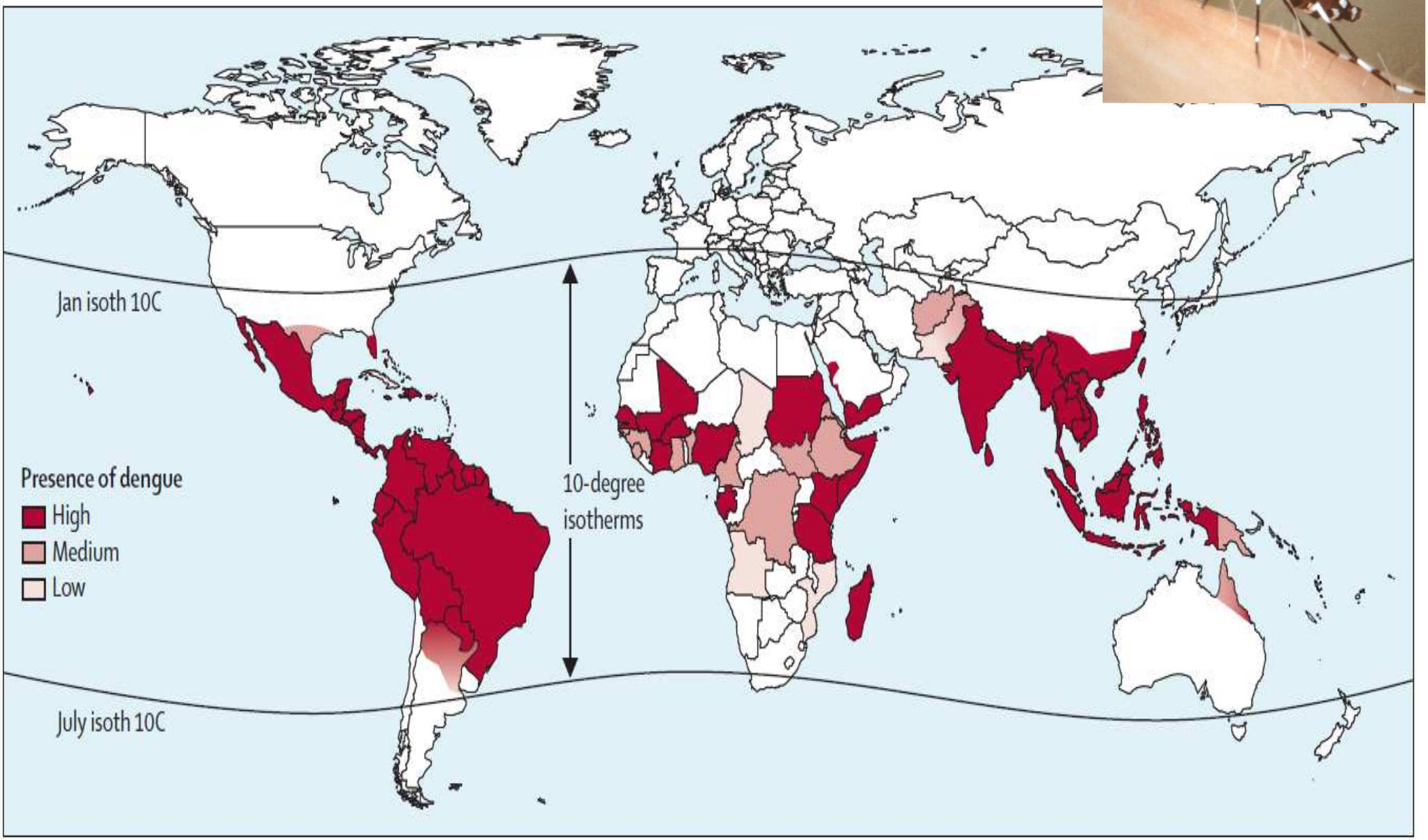
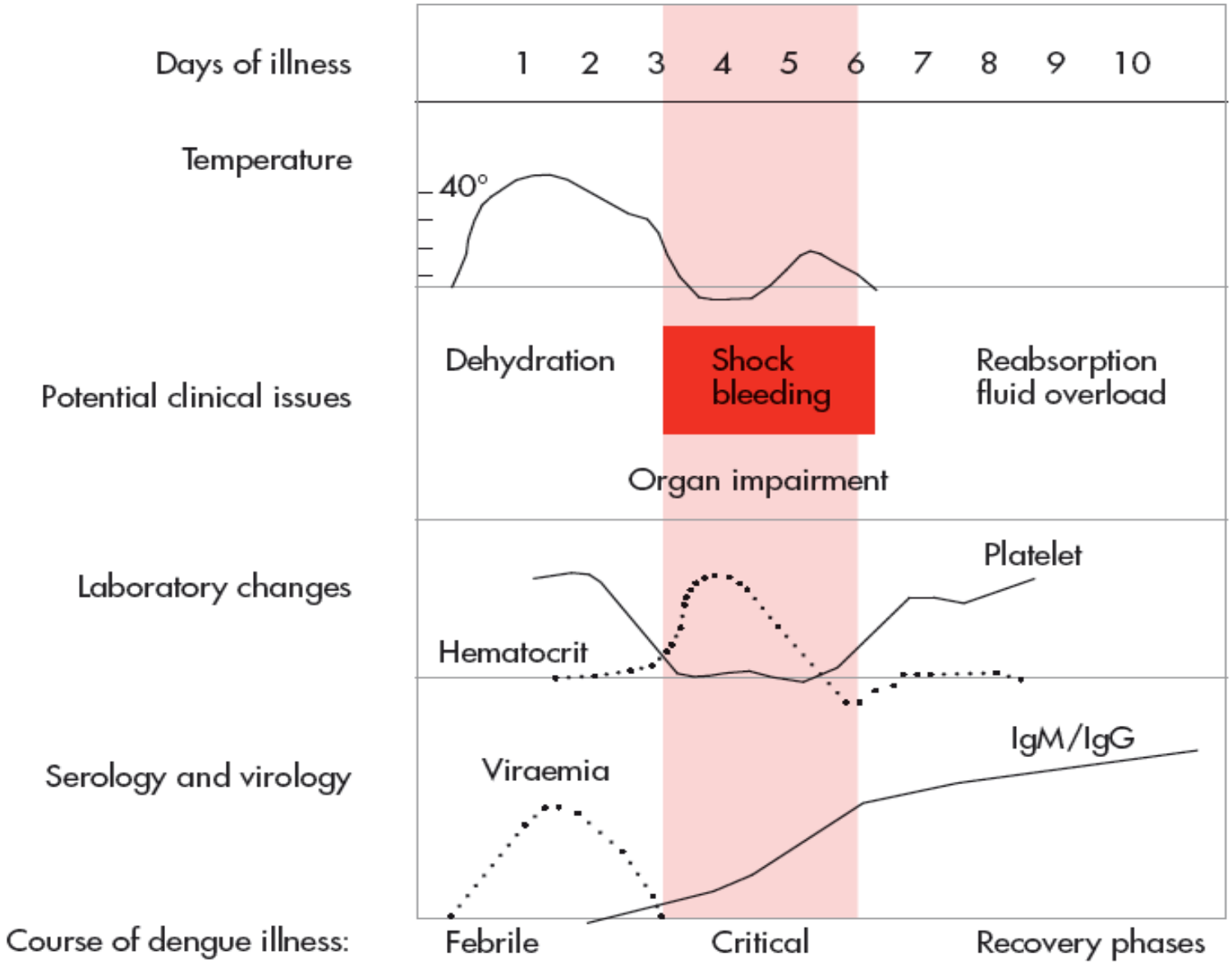


Figure 1: Global dengue burden, 2014

Data from Bhatt and colleagues,[1] Healthmap,[2] and WHO[3] were integrated to indicate the relative amount of dengue globally according to best estimates.

Dengue: course of disease



WHO guideline 2009

Dengue (n=64): clinical and laboratory predictors

	Adjusted LR+
• Leucopenia (< 4000/µL)	3.3
• Skin rash	2.8
• Thrombocytopenia (150,000/µL)	2.0

Bottieau et al. *Medicine* 2007

Dengue: diagnosis

- Serology (limitations ++)
- PCR for viremia (only reference centers)
- RDT NS1 dengue antigen
  - sensitivity = PCR (75-80%)

New

- RDT Combo NS1 Ag/serology
  - Sensitivity > 90%

Clinical added-value of dengue NS1 antigen RDT

Open Forum Infectious Diseases

MAJOR ARTICLE

Clinical Utility of the Nonstructural 1 Antigen Rapid Diagnostic Test in the Management of Dengue in Returning Travelers With Fever

Ralph Huits,[1] Patrick Soentjens,[1] Ula Maniewski-Kelner,[1] Caroline Theunissen,[1] Steven Van Den Broucke,[1] Eric Florence,[1] Jan Clerinx,[1] Erika Vlieghe,[1,2] Jan Jacobs,[1,3] Lieselotte Cnops,[1] Dorien Van Den Bossche,[1] Marjan Van Esbroeck,[1] and Emmanuel Bottieau[1]

[1]Department of Clinical Sciences, Institute of Tropical Medicine, Antwerp, Belgium; [2]Unit of Tropical Diseases, University Hospital of Antwerp, Belgium; and [3]Department of Microbiology and Immunology, University of Leuven, Belgium

- 355 febrile travelers evaluated
- 54 with dengue (16%)
- Sensitivity: 82.7%
- Specificity: 99.6%

Compared with historical controls

- Less hospital admissions
- Less empirical antibiotherapy

Dengue: management

The 2009 revised WHO dengue classification

DENGUE ± WARNING SIGNS | **SEVERE DENGUE**

Supportive treatment

CRITERIA FOR DENGUE ± WARNING SIGNS

Probable dengue

live in /travel to dengue endemic area.
Fever and 2 of the following criteria:

- Nausea, vomiting
- Rash
- Aches and pains
- Tourniquet test positive
- Leukopenia
- Any warning sign

Laboratory-confirmed dengue

(important when no sign of plasma leakage)

Warning signs*

- Abdominal pain or tenderness
- Persistent vomiting
- Clinical fluid accumulation
- Mucosal bleed
- Lethargy, restlessness
- Liver enlargment >2 cm
- Laboratory: increase in HCT concurrent with rapid decrease in platelet count

*(requiring strict observation and medical intervention)

CRITERIA FOR SEVERE DENGUE

Severe plasma leakage

leading to:

- Shock (DSS)
- Fluid accumulation with respiratory distress

Severe bleeding

as evaluated by clinician

Severe organ involvement

- Liver: AST or ALT >=1000
- CNS: Impaired consciousness
- Heart and other organs

Clinical distinction dengue – chikungunya – zika ?

Symptoms	Dengue	Chikungunya	Zika
Fever	++++	+++	+++
Myalgia/ arthralgia	+++	++++	++
Edema extremities	0	0	++
Maculopapular rash	++	++	+++
Retro-orbital pain	++	+	++
Conjunctivitis	0	+	+++
Lymphadenopathies	++	++	+
Hepatomegaly	0	+++	0
Leukopenia/thrombopenia	+++	+++	0
Hemorrhage	+	0	0

Ioos S et al. *Med Mal Infect*. 2014

ZIKV infection: clinical manifestations, travelers

ITM Feb-Nov 2016

zika (n=29)	n	%
rash	26	84
fever	17	55
artralgia	13	42
myalgia	5	16
conjunctivitis	2	6
diarrhoea	4	13
respiratory	2	6
fatigue	5	16

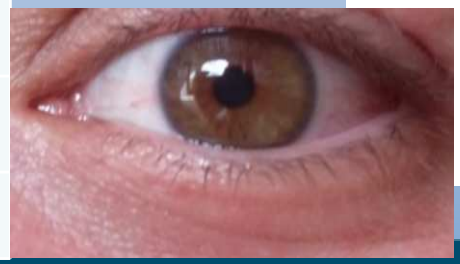
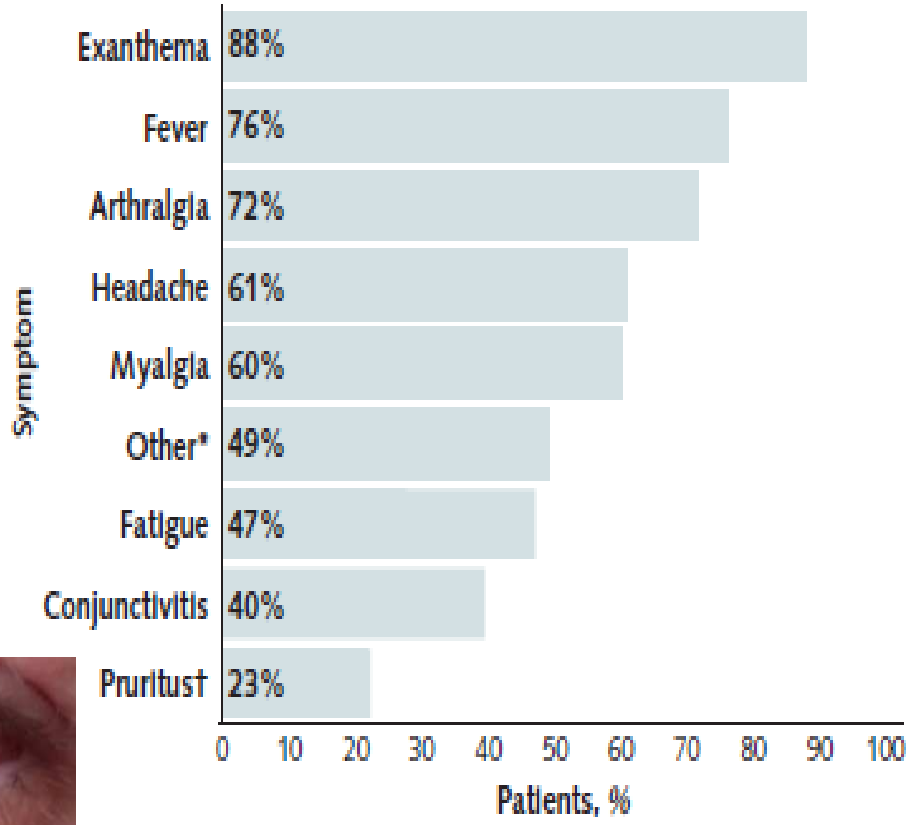
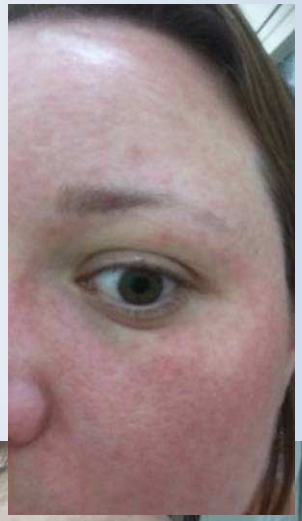


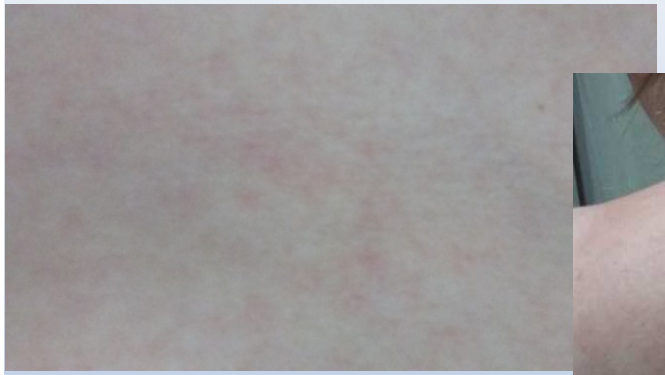
Figure 2. Clinical symptoms and signs among 93 patients diagnosed with Zika virus disease acquired in the Americas.



Hamer DH et. *Ann Intern Med* 2017

Day 2	Day 3	Day 4	Day 5	Day 6





Rickettsial infection in travelers

	ITMA, n=70 2000-2006 Bottieau *Medicine* 2007	GeoSentinel, n=261 1996-2008 Jensenius *Emerg Infect Dis* 2009
Spotted fever group *(R. africae, R. conorii,…)* **Tick-borne** 	63 (90%)	231 (88%)
Typhus group *(R. typhi)* **Flea-borne** 	4	10
Orientia tsutsugamushi **Mite-borne** 	3	16
Others/indeterminate	-	4

African tick bite fever (ATBF): diagnostic predictors

	Adjusted LR+
• Skin ulcers	11.1
• Skin rash	3.8

Bottieau et al. *Medicine* 2007

Rickettsial infection: management

- Diagnosis
  - Most of the time clinical (ATBF)
  - (Paired serology)
  - PCR on eschar, (serum/blood)

- Treatment
  - Doxycycline or
  - Azithromycine

Theunissen *et al. BMC Infectious Diseases* (2017) 17:273
DOI 10.1186/s12879-017-2385-x

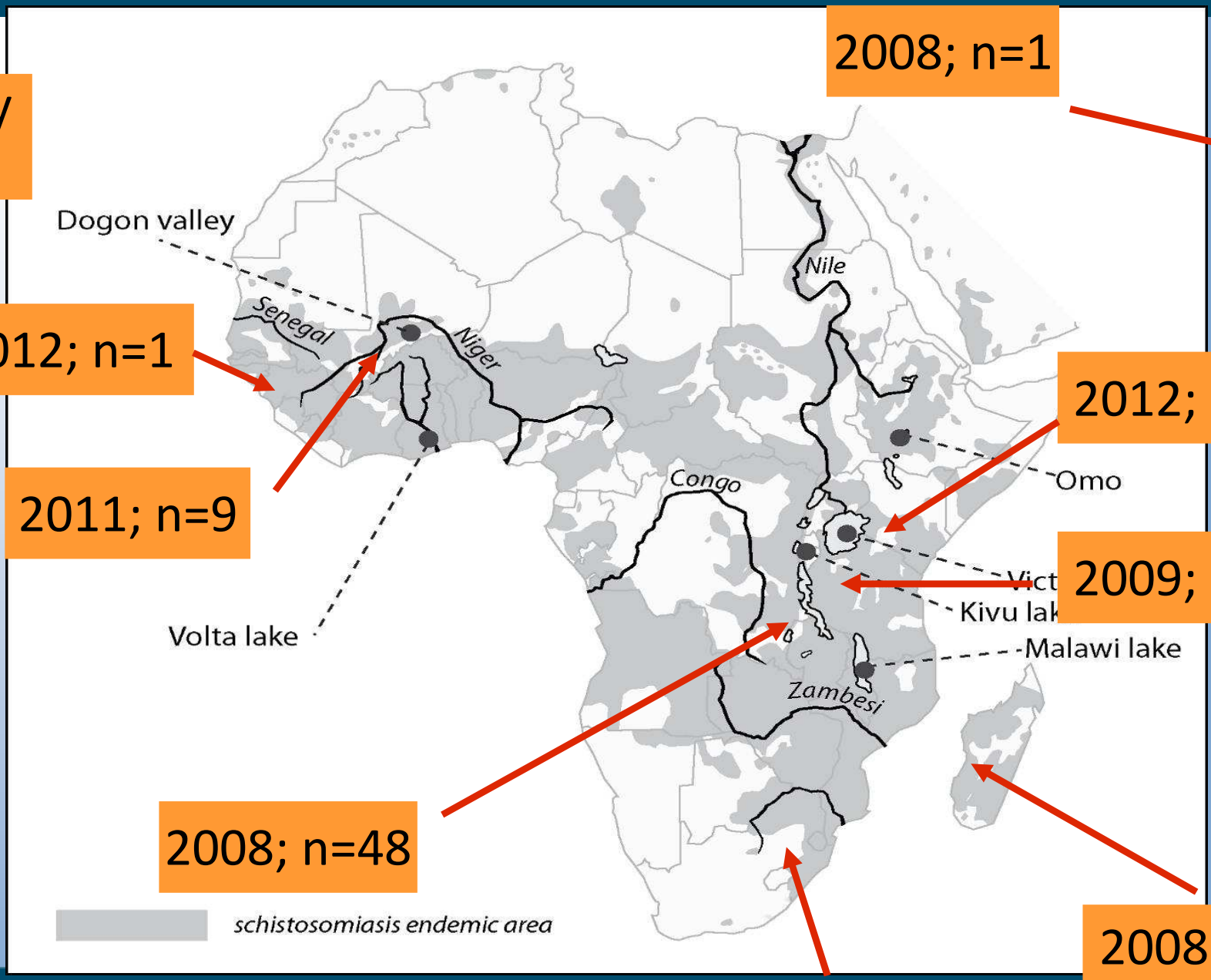
BMC Infectious Diseases

CASE REPORT Open Access

Acute-phase diagnosis of murine and scrub typhus in Belgian travelers by polymerase chain reaction: a case report

Acute schistosomiasis (Katayama) and travel

Seen recently at ITM

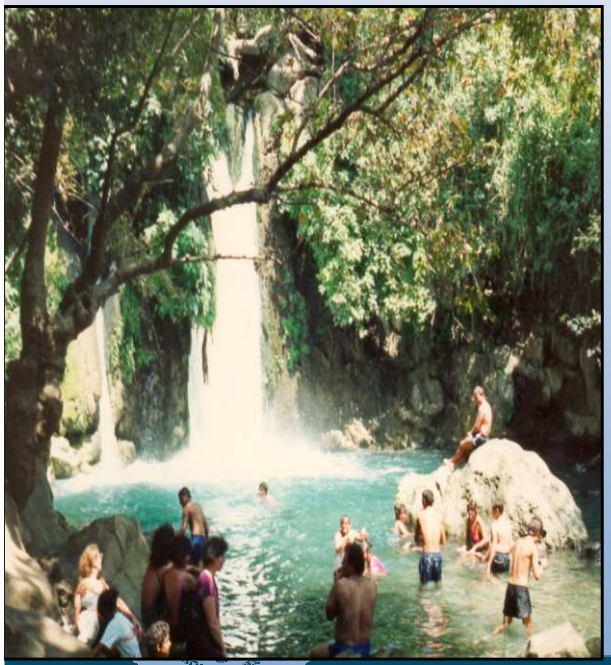


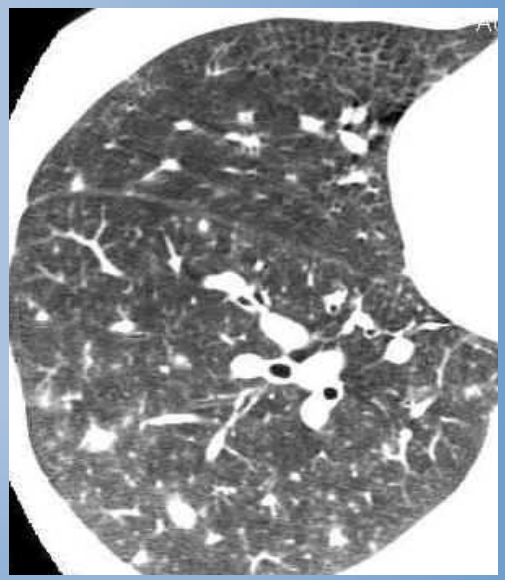
Clerinx J. *Trav Med Infect Dis* 2011

2017; n= 34

Katayama fever (n=38): diagnostic predictor

	Adjusted LR+	Adjusted LR-
• Eosinophil count > 500/µL)	32	0.06





Bottieau et al. *Medicine* 2007

Katayama fever: diagnosis

Journal of
TRAVEL MEDICINE

ORIGINAL ARTICLES

Acute Schistosomiasis in a Cluster of Travelers From Rwanda: Diagnostic Contribution of Schistosome DNA Detection in Serum Compared to Parasitology and Serology

Jan Clerinx, MD,* Emmanuel Bottieau, MD,* Dominic Wichmann, MD,†‡
Egbert Tannich, MD,† and Marjan Van Esbroeck, MD*

Wichmann *et al. BMC Infectious Diseases* 2013, **13**:55
http://www.biomedcentral.com/1471-2334/13/55

BMC Infectious Diseases

RESEARCH ARTICLE Open Access

Prospective European-wide multicentre study on a blood based real-time PCR for the diagnosis of acute schistosomiasis

Dominic Wichmann[1*], Sven Poppert[2], Heidrun Von Thien[2], Joannes Clerinx[3], Sebastian Dieckmann[4], Mogens Jensenius[5], Philippe Parola[6], Joachim Richter[7], Mirjam Schunk[8], August Stich[9], Philipp Zanger[10], Gerd D Burchard[2,11] and Egbert Tannich[2]

	n=13	n=37
•Egg detection:	69%	25%
•Serology:	77%	72%
•Serology AND egg detection:	85%	
•**Serum *Schistosoma* DNA (PCR):**	**100%**	**95%**

Clerinx J et al. *J Trav Med* 2011; **Wichmann D et al**. *BMC Infect Dis* 2013

Katayama fever: treatment

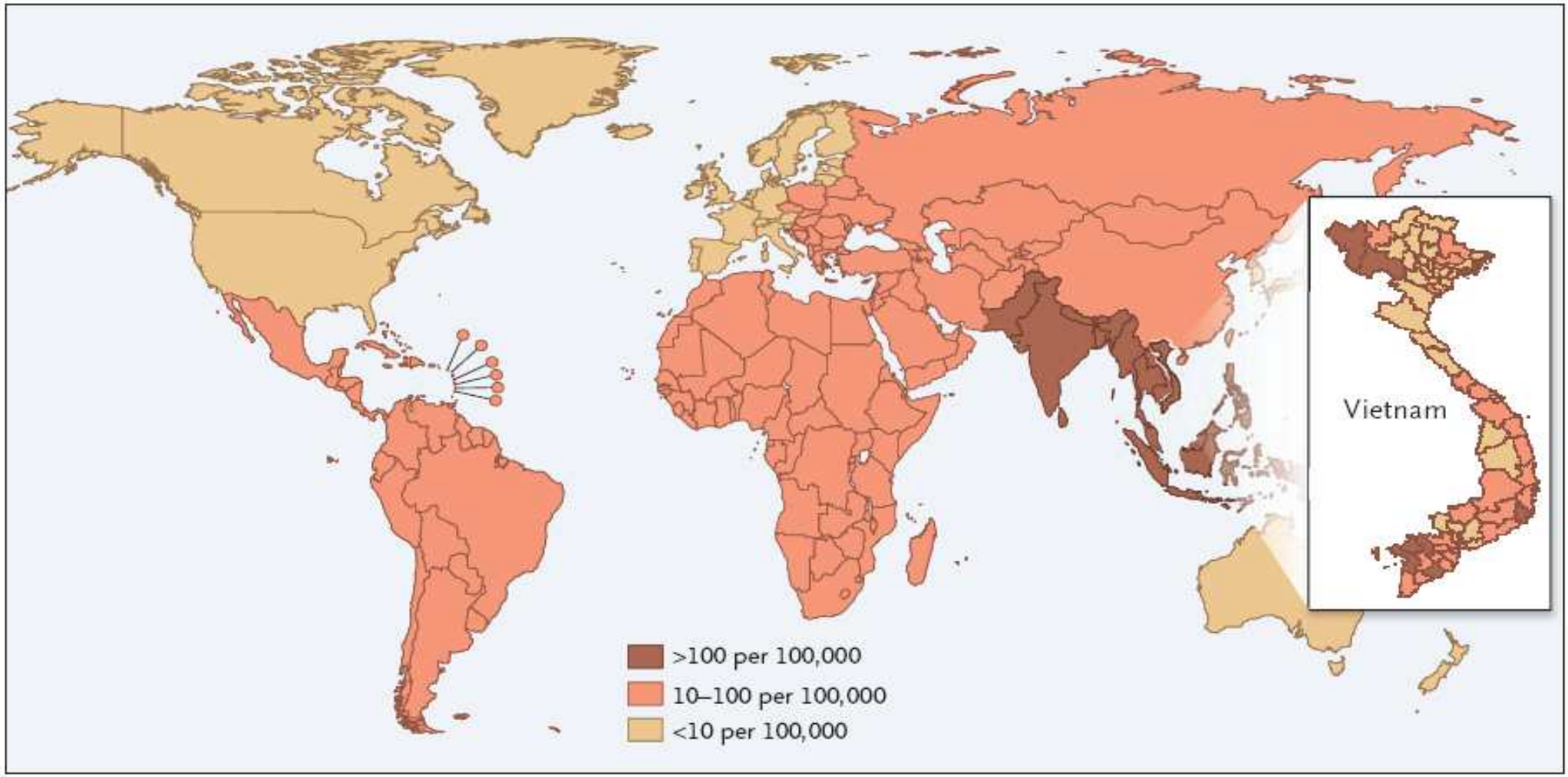
Controversial

- Symptomatic (NSAID or corticosteroids)
  - Followed by praziquantel (PZQ: 40 mg/kg single dose) 6-12 weeks later

OR

- Praziquantel at diagnosis
  - But clinical exacerbation (about 50%)
  - To combine with corticosteroids (2-3 days PZQ in such cases)
  - To repeat after 6 weeks to 3 months

Enteric fever (*Salmonella* Typhi and Paratyphi A).



Mean Annual Incidence of Typhoid Fever per 100,000 Persons.

Country-specific incidence rates, some of which are estimates, are for 2000. Province-specific incidence rates for Vietnam are for children 5 to 14 years of age, between 1999 and 2003 (inset). Country data are from Crump et al.[2] Provincial data for Vietnam are from a meta-analysis conducted by the DOMI Program.

DeRoeck D et al. *N Engl J Med* 2007; **Crump JA et al.** *Bull World Health Organ* 2004

Enteric fever: ITMA experience 2006-2011

- Diagnosis by blood culture
- *S.* Typhi (n=9) and *S.* Paratyphi A (n=14)
- Indian subcontinent/southeast Asia : 17 (74%)
- Resistance to acid nalidixic: 9/14 (64%)
  - Corresponding to “decreased cipro susceptibility” (MIC>0.064 µg/ml), and risk of clinical failure
- Empirical choice: ceftriaxone or azithromycine

Enteric fever (n=15): diagnostic predictors

	Adjusted LR+
• Enlarged spleen	10
• Raised transaminases	2.5

Example: skin rash in a febrile returning traveler

From Africa

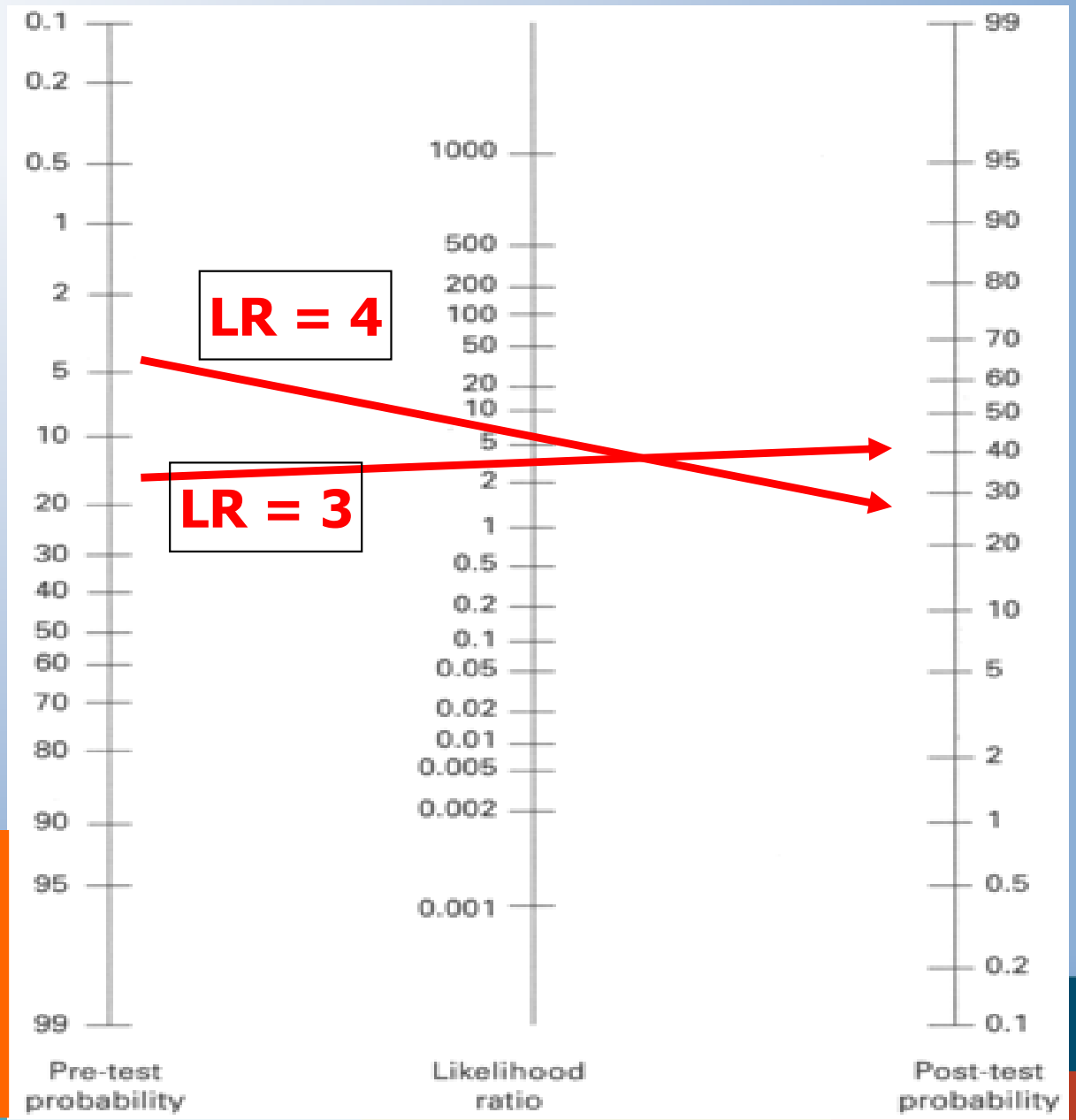
Rickettsiosis ?

5%

From Asia

Dengue ?

15%

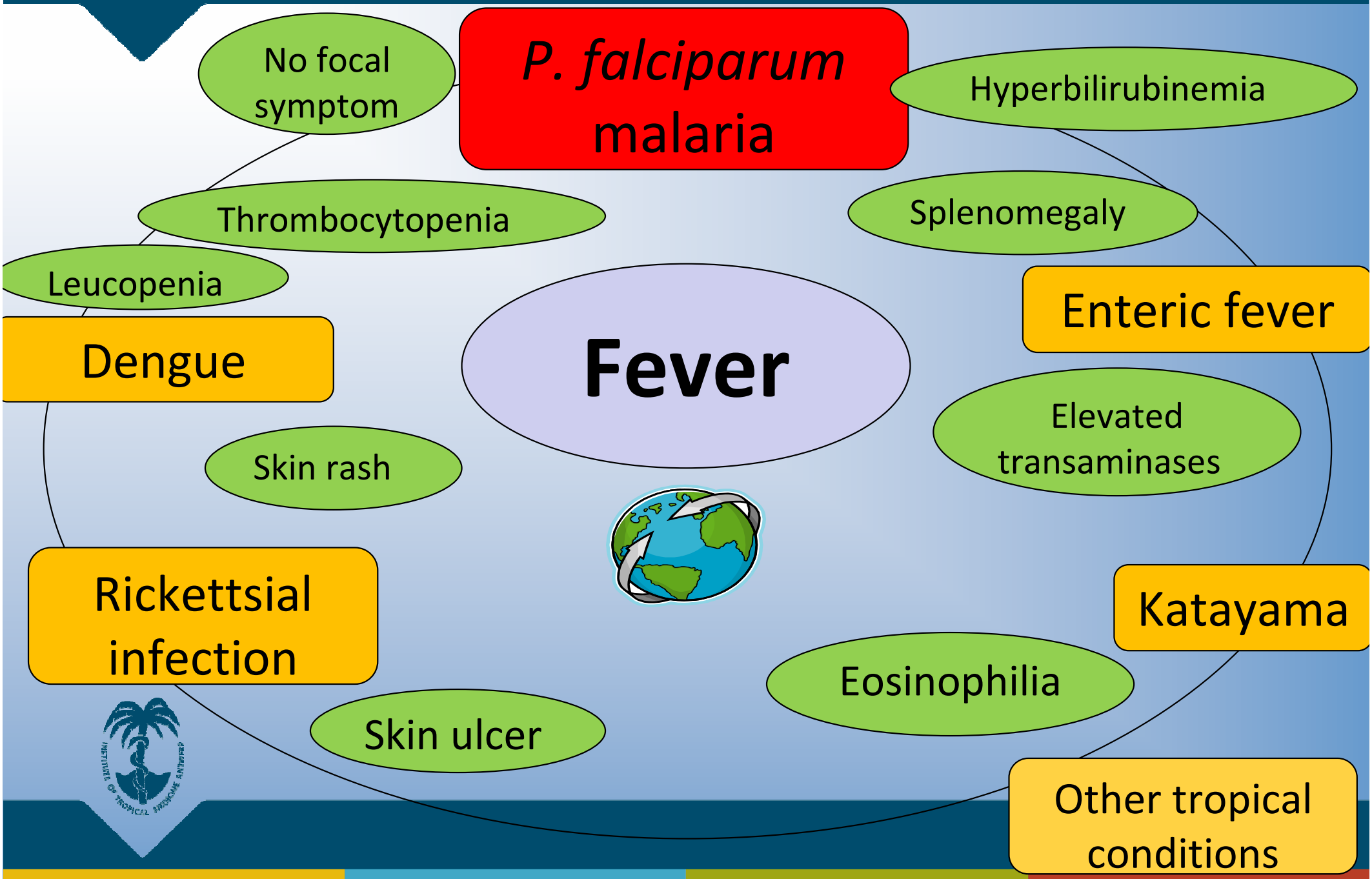


40%

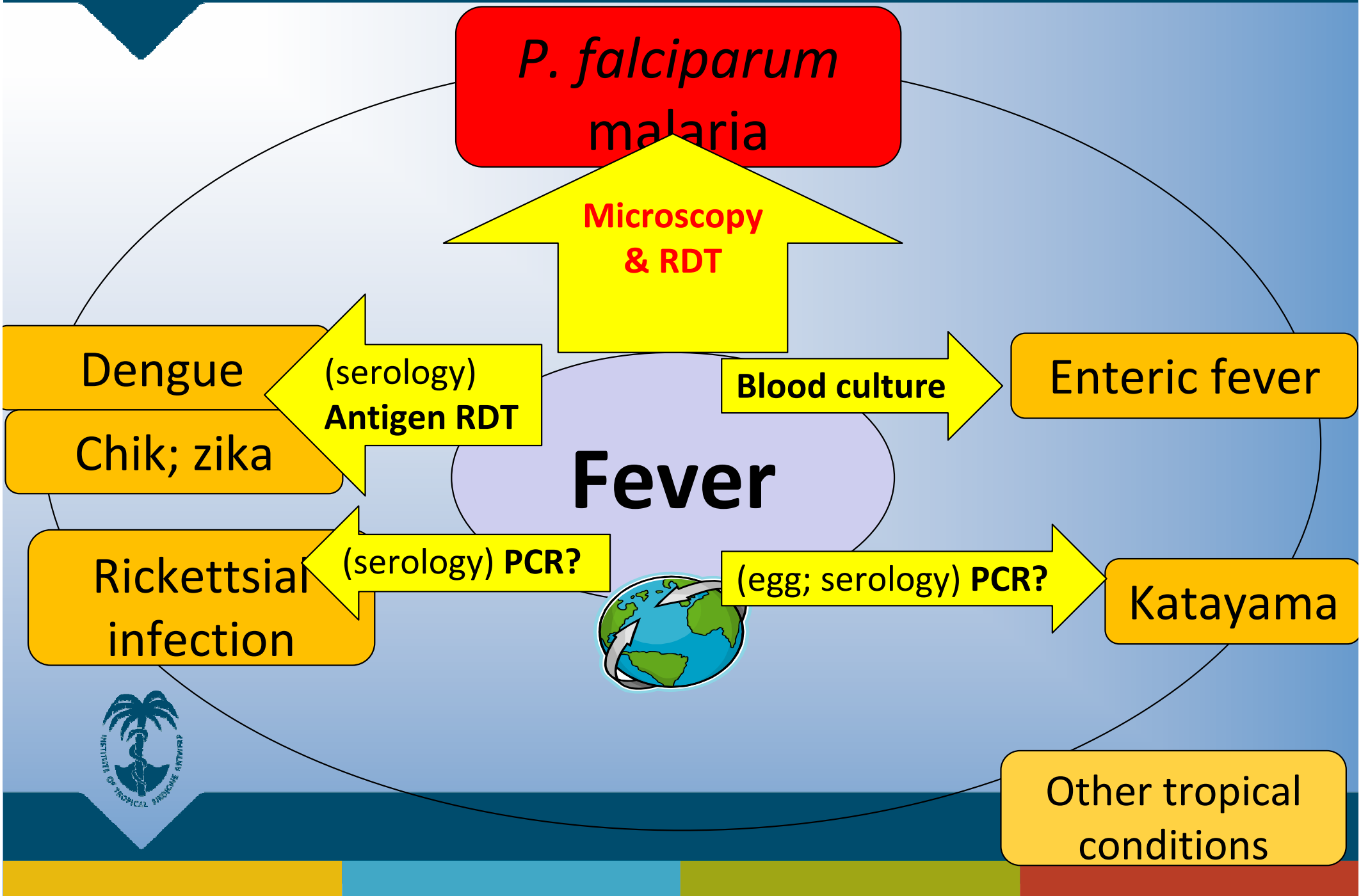
20%

Fagan nomogram

Conclusion fever and travel: diagnostic panorama



Conclusion fever and travel: tools for early diagnosis



Gracias por la atencion

Interesting websites/diagnostic aids

- GIDEON at www.gideononline.com
- FEVERTRAVEL at www.fevertravel.ch
- KABISA TRAVEL at www.kabisa.be