

EMERGING RICKETTSIAL DISEASES OF THE THAI-MYANMAR BORDER

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STUDY SITE (1)

THAILAND

Thai-Myanmar border

**Kanchanaburi Province
Sangkhlaburi District**

**Ethnic groups:
Karen, Mon, Thai, Burmese**



STUDY SITE (2)



STUDY SITE (3)



BACKGROUND

Rickettsial Diseases in Sangkhlaburi (1)

CLINICAL SUSPICION: ESCHAR AND / ORRASH



BACKGROUND

Rickettsial Diseases in Sanghklaburi (2)

The AFRIMS/ Kwai River Clinical Center Fever Project

FIRST 150 FEBRILE VOLUNTEERS ENROLLED (JULY 1999-FEBRUARY 2000)

- 3%: SEROCONVERSION FOR SFG RICKETTSIOSES (IF WITH *R. RICKETTSII*)
- SFG ANTIBODIES: 9%
- SEROPREVALENCE OF *EHRlichia* spp. :

E. CHAFFEENSIS 3 %

A. PHAGOCYTOPHILA 5 %



OBJECTIVES

AFRIMS STUDY OF THE ETIOLOGY OF UNDIFFERENTIATED FEVER SYNDROMES IN
SANGKHLABURI DISTRICT

DETERMINE WHETHER

HUMAN EHRLICHIOSIS AND / OR SFG RICKETTSIOSIS

MAY SERVE AS ETIOLOGIC AGENTS FOR FEVERS



MATERIAL AND METHODS (1): Patients

PATIENTS RECRUITED FROM THE POPULATION OF ADULTS WHO PRESENT TO KRCH FOR:
ORAL TEMPERATURE $\geq 38^{\circ}\text{C}$ OR WITH HISTORY OF FEVER DURING THE PAST 48 HOURS.
PARTICULARLY IF RASH, ARTHROPOD BITE OR ESCHAR

Exclusion Criteria:

- FOLLOW UP BASIS FOR A KNOWN CAUSE OF FEVER
- CONTINUATION OF TREATMENT OF A KNOWN FEVER-ASSOCIATED DISEASE
- PATIENTS UNWILLING OR UNABLE TO PROVIDE BLOOD SAMPLES 2-6 WEEKS AFTER THE DAY OF ENROLLMENT



MATERIAL AND METHODS (2): Samples

(WRAIR PROTOCOL 745,S96)

Blood Sampling:

6.5 cc ACD for routine laboratory investigation, molecular assays and rodent inoculation

5 cc (clotted) to be fractionated, sera used for immunofluorescent serology and western-blot

1 cc (heparinized) for isolation in cell-culture systems

Skin biopsy of rash and/or eschar

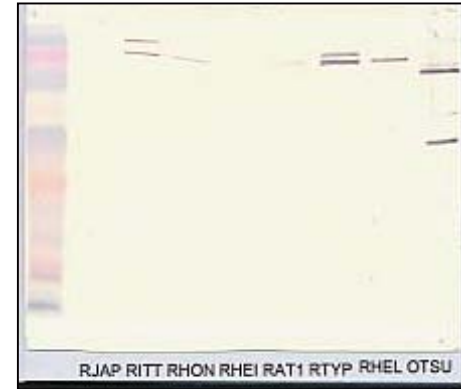
SENTIUNITÉ DES RICKETTSIES
PR D. RAOUL
WHO COLLABORATIVE CENTER FOR
RICKETTSIAL REFERENCE AND
RESEARCH IN MARSEILLE
FRANCE



MATERIAL AND METHODS (3): Testing

Diagnostic tools:

- **IF serology** using a panel of 13 rickettsial antigens acute and convalescent (Day 21) samples completed by Western blot
- **PCR detection** using OmpA and gltA specific primers (*Rickettsia* sp.) 16SRNA gene primers (*Ehrlichia* sp.)
- **Cell culture** by the shell-vial technic



RESULTS

14 CONFIRMED RICKETTSIOSES

- 3 cases of **murine typhus** (*R. typhi*)
- 3 cases of **scrub typhus** (*O. tsutsugamushi*)
- 8 cases of **SFG rickettsioses** (?)



3 cases of murine typhus: *R. typhi*

| N° AFRIMS | Age (y) | Clinical particularities | | | | | IF <i>R. typhi</i> TITERS IgG/IgM |
|--------------|------------|--------------------------|-----------------|--------|-----------------|--|---|
| | | Fever | Diffuse rash | Eschar | Local nodes | Other | |
| H199 | 35 | YES | NO | NO | FEMORAL LEFT | CHILLS HEADACHE | N°1: 16/256 N°2: 512/256 |
| H431 | 37 | YES | NO | NO | NO | CHILLS HEADACHE NAUSEA VOMITING | N°1: 64/8 N°2: 512/256 |
| H444 | 20 | YES | NO | NO | NO | HEADACHE | N°1: 0/64 N°2: 128/256 |

Cases of scrub typhus (1): H 535



35-YEAR-OLD THAI MAN

**SEVERE: 3-DAY FEVER
+ CHILLS + HEADACHE + VOMITING**

FAILURE OF A 5-DAY CEFTRAXONE

RECOVERED WITH DOXYCYCLINE

REMOVED MULTIPLE ARTHROPODS AFTER JUNGLE TRIPS



H 535: multiple bites



H 535: diagnosis

SEROLOGY IF (IGG/IGM)

O. TSUTSUGAMUSHI GILLIAM

KARP

KATO

KAWAZAKI

R. JAPONICA

R. HELVETICA

R. HONEI

ACUTE

0/32

0/8

0/0

0/8

0/16

0/16

0/8

LATE

256/32

256/32

0/0

0/8

0/16

0/16

0/8

PCR BIOPSY: NEGATIVE

BIOPSY/BLOOD CULTURE: NEGATIVE



Cases of scrub typhus (2): H 541



50-YEAR OLD MONWOMAN

3-DAY FEVER + CHILLS
ESCHAR + RASH

AFTER GRASS CUTTING
CHRONIC ALCOHOLISM
NO BITE NOTICED

RECOVERED
WITH DOXYCYCLINE TRT



H 541: 3 eschars



SHOULDER: 4 CM



LEFT CALF: 3 CM



RIGHT CALF: 4 CM



H 541: Macular rash



H 541: diagnosis

SEROLOGY IF (IGG/IGM)

O. TSUTSUGAMUSHI GILLIAM

KARP

KATO

KAWAZAKI

R. JAPONICA

R. HELVETICA

R. HONEI

ACUTE

128/64

0/0

0/0

0/0

0/32

0/32

0/16

LATE

128/16

0/0

0/0

0/0

0/32

0/32

0/16

PCR BIOPSY: NEGATIVE

BIOPSY/BLOOD CULTURE: NEGATIVE



Cases of scrub typhus (3): H 548

42-YEAROLD MONIMAN

3-DAY FEVER + CHILLS
+ HEADACHE

MULTIPLE BITES AFTER
A TRIP INTO THE JUNGLE

RECOVERED
WITH DOXYCYCLINE TRT



H 548: multiple bites



H 548: diagnosis

SEROLOGY IF (IGG/IGM)

O. TSUTSUGAMUSHI GILLIAM

KARP

KATO

KAWAZAKI

R. JAPONICA

R. HONEI

R. HELVETICA

ACUTE

0/0

0/0

0/0

0/0

0/0

0/8

0/16

LATE

512/128

512/0

0/0

0/0

16/16

0/8

16/16

PCR BIOPSY: NEGATIVE

BIOPSY/BLOOD CULTURE: NEGATIVE



8 cases of SFG rickettsioses (1)

| | Age | Comments | Fever | Rash | Eschar | Nodes | Other | SFG IgG/Ig M | WB |
|------|-----|-------------------------------|-------|------|---------------------|-------|--|---|----|
| H111 | 50 | Severe | Yes | Yes | Yes Left Knee | No | Chills Abdom. Rales Confus. Tpenia Anemia | <i>R. conorii</i> Indian N°1: 128/16 N°2: 128/16 | + |
| H131 | 45 | Severe Jungle trips | Yes | No | No | No | Nausea Vomiting Diarrhea HMG SPM | <i>R. conorii</i> Indian N°1: 64/32 N°2: 64/32 | + |

8 cases of SFG rickettsioses (2)

| | Age | Comments | Fever | Rash | Eschar | Nodes | Other | SFG IgG/Ig M | WB |
|-------------|-----------|---|------------|-----------|--|-----------|--|---|----------|
| H380 | 35 | Jungle trips Severe Tick bite one week before | Yes | No | Yes heaped edge 0.8 cm | No | Chilliness Headache Nausea vomiting Coughing Myalgia HMG WBC 14 | R. helvetica N°1: 64/256 N°2: 16/128 | + |
| H191 | 37 | “Insect” entered the left ear ? | Yes | No | No | No | Chilliness Headache Nausea vomiting Coughing Myalgia WBC 19.8 GGT 168 ALT 88 | R. helvetica N°1: 0/16 N°2: 128/32 | + |

8 cases of SFG rickettsioses (3)

| | Age | Fever | Rash | Eschar | Nodes | Other | SFG IgG/IgM | WB |
|-------------|-----|-------|------|--------|-------|---|--|----|
| H046 | 53 | Yes | No | Yes | No | Chilliness Chills Headache Myalgia | SFG: Rh / Rc ? N°1: 32/8 N°2: 64/8 | + |
| H284 | 70 | Yes | No | No | No | Chilliness Headache Nausea vomiting Abdominal pain HMG Anemia Hb 9 | SFG: Rh / Rc ? N°1: 0/32 N°2: 32/32 | + |
| H207 | 28 | Yes | No | No | No | Chilliness Headache Nausea vomiting Resp. Myalgia | Rh: N°1: 16/128 N°2: 16/64 Rt: N°1: 64/128 N°2: 32/32 | + |

8 cases of SFG rickettsioses (4): H 492



49-YEAR-OLD KAREN WOMAN
3-DAY FEVER + CHILLS

RETROSPECTIVE QUESTIONING:
REMOVED A TICK
FROM HER BODY
10 DAYS PRIOR FEVER



H 492: tick-bite eschar



**3 WEEKS
AFTER REMOVING THE TICK**



H 492: diagnosis

SEROLOGY IF (IGG/IGM)

R. HELVETICA

R. HONEI

R. CONORII

ACUTE

64/16

128/0

64/8

LATE

32/16

64/0

32/8

PCR BIOPSY: NEGATIVE

BIOPSY/BLOOD CULTURE: NEGATIVE



In process: Cross absorption studies

TIQ. THAILANDE : R. JAP R. ITT R. HON R. HEI R. AT1 R. TYP R. HEL O.TSU

Serum n° : 2111888 13 / THAILANDE



Serologie :

| | |
|--------|--------|
| R. JAP | 16/8 |
| R. ITT | 0/16 |
| R. HON | 16/256 |
| R. HEI | 32/32 |
| R. AT1 | 0/32 |
| R. TYP | 0/256 |
| R. HEL | 64/256 |
| O.TSU | 0/0 |

RJAP RITT RHON RHEI RAT1 RTYP RHEL OTSU



CONCLUSION



CONCLUSION (1)

Rickettsial diseases are causes of fever in the

Thai-Myanmar border:

- **Murine typhus**
- **Scrub typhus**
- **SFG rickettsioses**



CONCLUSION (2)

SFG RICKETTSIOSES: WHAT IS THE CAUSATIVE *RICKETTSIA*?

- *R. HOWE* AND THAI TICK TYPHUS *RICKETTSIA*:
ASSOCIATED WITH TICKS IN THAILAND
NOT INVOLVED IN THESE CASES
- *R. CONY* / INDIA ? *R. HELVETICA* ?
- OTHER CROSS REACTING *RICKETTSIA* ?



CONCLUSION (3)

Human Ehrlichioses ?

- NOT DEMONSTRATED
- SEVERAL NEW EHRlichIAE DETECTED FROM TICKS

POSTER SESSION: ABSTRACT 456



CONCLUSION (3)

**Empiric treatment of patients
with unspecific febrile diseases**

Place of a 7-day doxycycline treatment ?



ACKNOWLEDGMENTS (1)

- DR. CHANSUDA WONGSRICHANALAI, DR. R. SCOTTMILLER AND THE AFRIMS FEVER STUDY TEAM
- DR. PHIL MCDANIEL AND KRCH TEAM
- AFRIMS VETMED TEAM.
- DR. SAM R. TELFORD, HSPH
- PR. DIDIERRAOUT, UNITÉ DES RICKETTSIES



ACKNOWLEDGMENTS (2)

THIS WORK WAS SUPPORTED THE US DEPARTMENT OF DEFENSE – GLOBAL EMERGING INFECTIONS SURVEILLANCE PROGRAM (DOD-GEIS)

PERSONAL FUNDING:

- FONDATION BAYER SANTÉ
- MINISTÈRE FRANÇAIS DES AFFAIRES ÉTRANGÈRES (PROGRAMME LAVOISIER)
- FONDATION POUR LA RECHERCHE MÉDICALE
- ASSISTANCE PUBLIQUE – HÔPITAUX DE MARSEILLE
- INSTITUT DE RECHERCHE INTERNATIONALE SERVIER
- ASSOCIATION DES PROFESSEURS DE PATHOLOGIE INFECTIEUSES ET TROPICALES
- EUROPEAN SOCIETY OF CLINICAL MICROBIOLOGY AND INFECTIOUS DISEASES

