



Public Health  
England



# Spots, ticks, fleas and chiggers

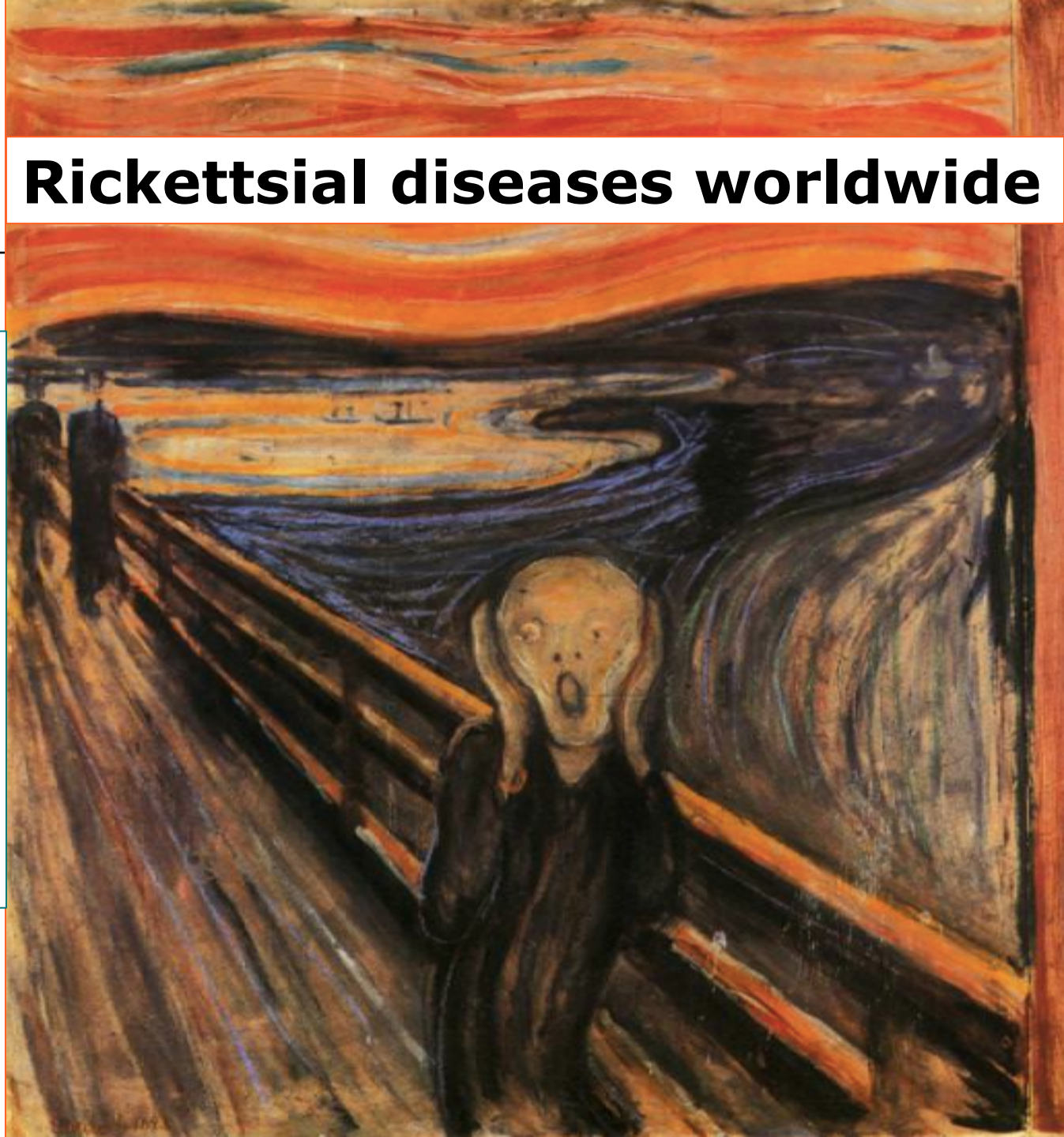
Dr Laura Nabarro



# Rickettsial diseases worldwide

## Confusing

- Uncommon
- Many diseases
- Similar names
- Multiple names
- Similar clinical syndromes
- Geographically specific
- Difficult to diagnose





# Similarities (1)

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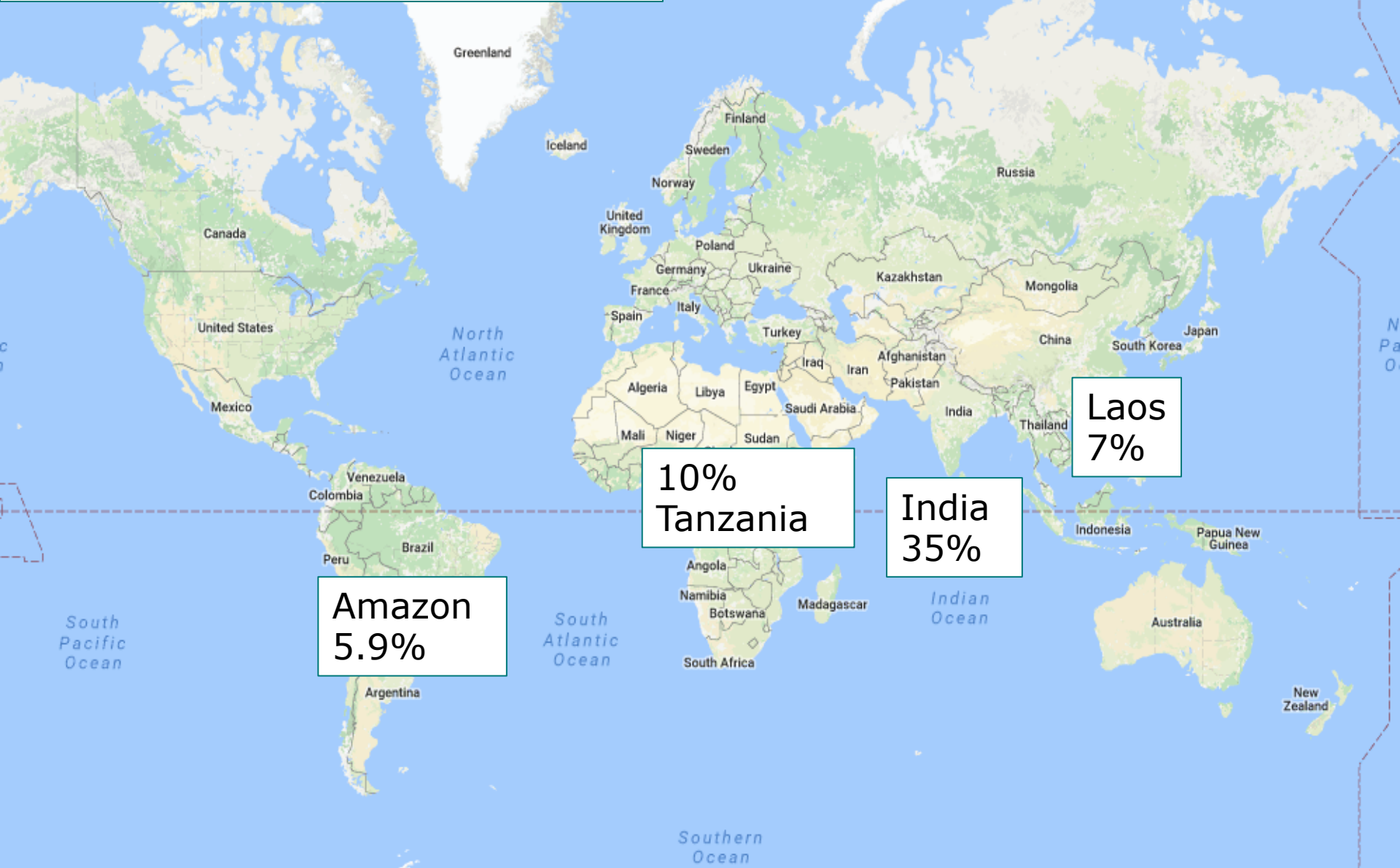
- Gram negative cocco-bacilli
- Obligate intracellular pathogens
  - invade endothelial cells
  - vasculitic syndrome

## Similarities (2)

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- All spread by arthropods
  - Vectors: fleas, mites, lice, ticks
    - Often also act as reservoir
  - Reservoir: small mammals / birds
- Present all around the world
  - Worldwide distribution eg murine typhus
    - cosmopolitan host and vector
  - Geographically restricted eg scrub typhus
    - Specific environmental conditions of hosts and vectors

- # Returning travellers
- 5- 26.6% of travellers with fever from sub-Saharan Africa
  - 2-3% febrile travellers from Asia





## Similarities (3)

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- Incubation 6 - 14 days (< 21 days)
- Fever, malaise, headache, myalgia
  - No apparent focus of infection
  - Eschar?
  - Rash?
  - Severe - vasculitic syndrome
- Variable severity



# Similarities (4)

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## ○ Bloods

- Normal white cell count
- Normal or low platelets
- CRP elevated
- Normal or slightly elevated ALT/  
bilirubin
- Renal failure and DIC late



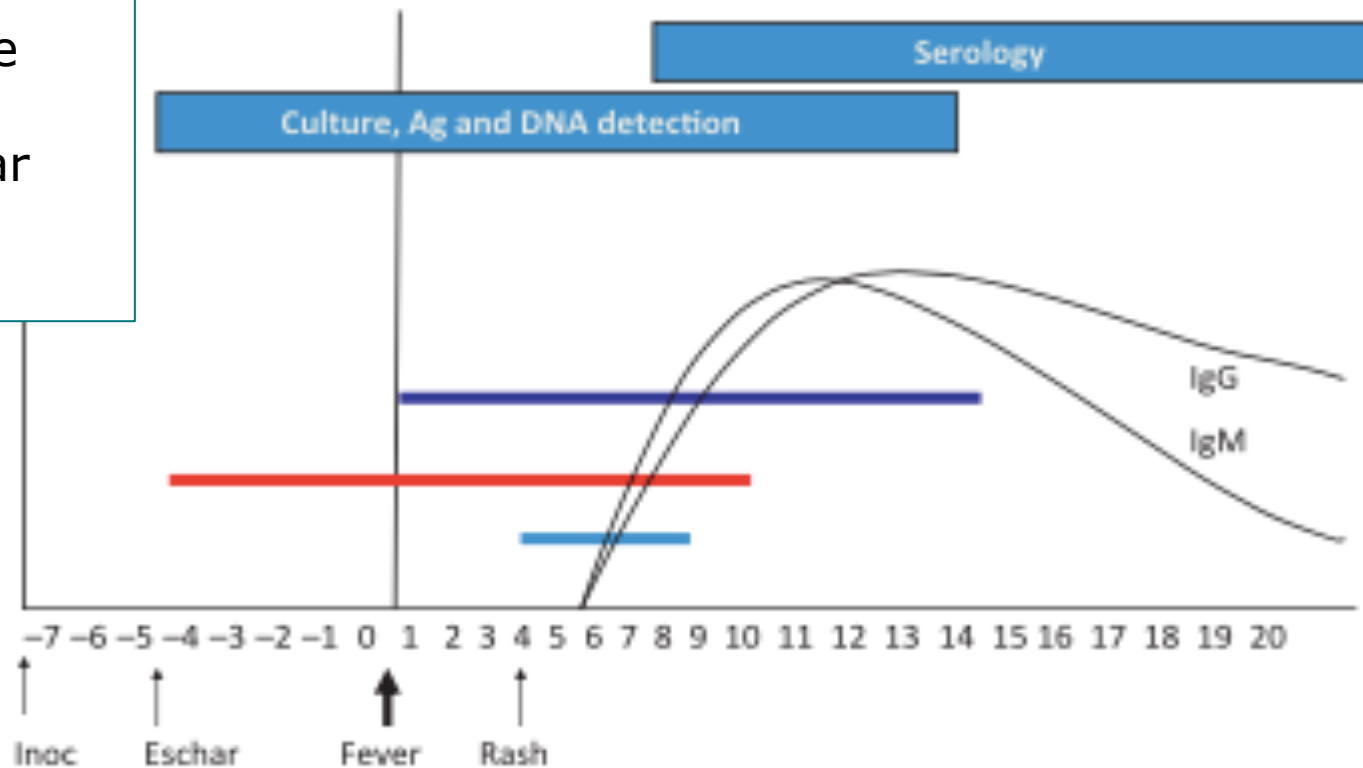
## Similarities (5)

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- Difficult to diagnose
  - Very hard to culture
  - Short rickettsaemic period
  - Delayed seroconversion

# Similarities (6)

- PCR
  - Whole blood
  - Eschar
  - Rash
- Serology



Richards et al. Worldwide detection and identification of new and old rickettsiae and rickettsial diseases. FEMS Immunol Med Microbiol 64 (2012) 107–110

# Similarities (7)

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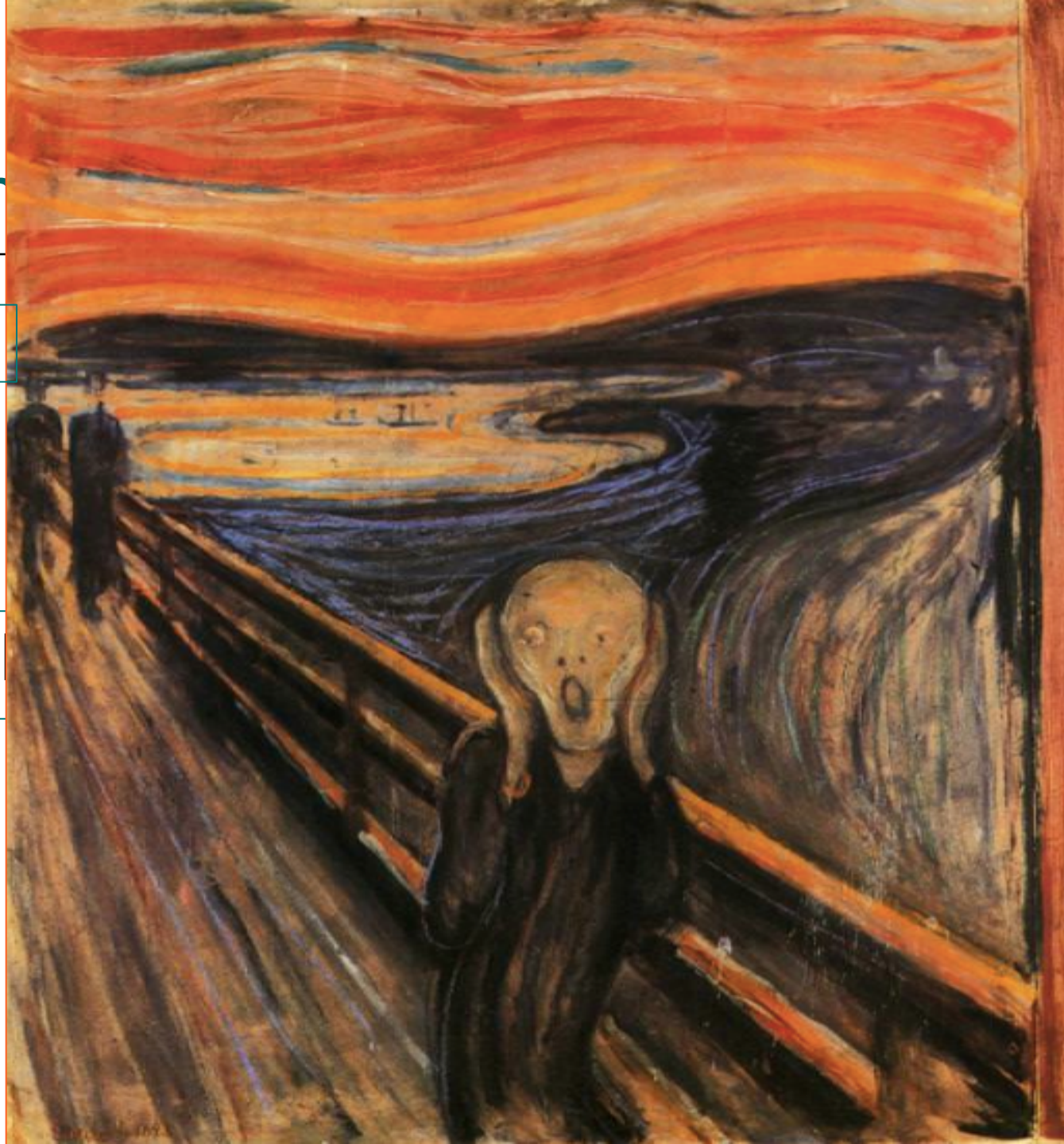
- Gold standard: Doxycycline
  - PO vs IV
- Alternatives
  - Chloramphenicol
    - Side effects
  - Macrolides
    - No *in vivo* data in RMSF or murine typhus
  - Fluroquinolones
    - Not all species are susceptible

# Termin

Epidemic

Typ

Cat flea fever



# Terminology: 3 groups

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- Spotted fever

- African spotted fever
- Mediterranean spotted fever
- Rocky mountain spotted fever
- + many more

- Scrub typhus

- Typhus group

- Epidemic typhus
- (Endemic)  
Murine typhus



## Similarities (7)

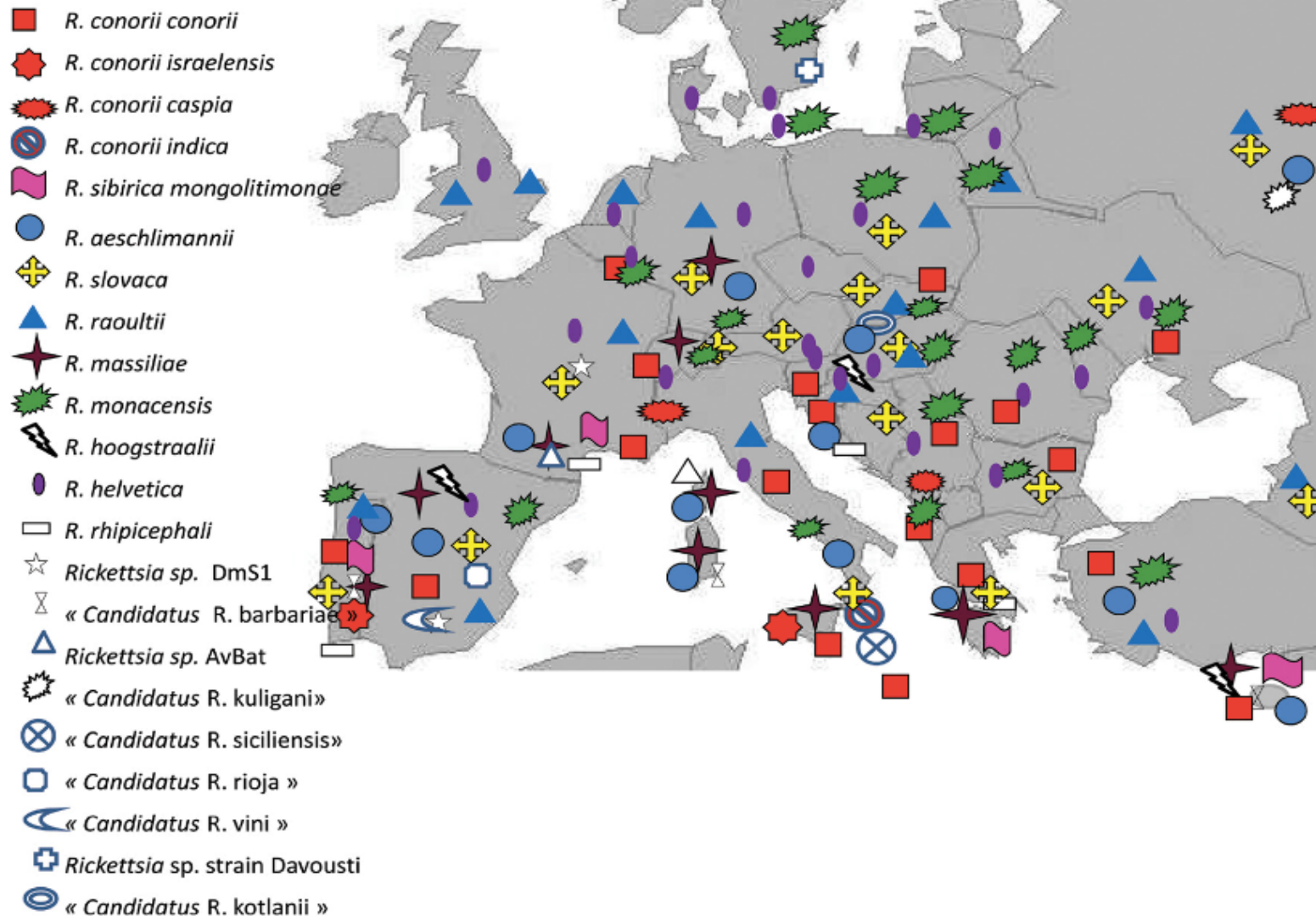
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- Serology- group specific
  - ET IgM and IgG IFAT
  - SF IgM and IgG IFAT
  - Scrub typhus- ELISA
- Cross-react
  - Coxiella
  - Bartonella

# Spotted Fevers

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- Many different species worldwide
  - Ever expanding group
- Classically tick borne
  - Many patients have no history of tick bite
- Incubation 6-10 days (<21d)
- Environment in which humans become infected depends upon the habitat and biting behaviour of the tick species



# Clinical features

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- Fever, headache, myalgia
- Local lymphadenopathy
- Inoculation eschar
  - Variable prevalence
  - If present, diagnostic
- Rash
  - Macular or maculopapular
  - Can be spotless

Mild

## *Rickettsia africae*

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- African tick bite fever/ spotted fever/ tick typhus
- *Ambylomma varigatum*
- Geographical confines- Africa/Caribbean
- Ticks aggressively seek host
- Common cause of FIRT- tourist clusters
- Usually mild disease
  - Fever, headache, myalgia
  - Eschars common, may be multiple

Other mild spotted fever

- Flinders Island spotted fever – *R. honei*

Moderate

# *Rickettsia conorii*



## *Rickettsia conori*

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- Mediterranean spotted fever / Boutonneuse fever
- *Rhipicephalus sanguineus*
  - Sporadic cases, often in urban/ suburban areas
- Europe, Africa, Asia
- More severe than African tick typhus
  - Eschar common, usually single
  - Untreated mortality of 3-30%

### Other moderate severity spotted fevers

- Queensland tick typhus – *R. australis*
- Siberian spotted fever – *R. siberica*
- Japanese spotted fever – *R. japonica*

# *Rickettsia rickettsii*

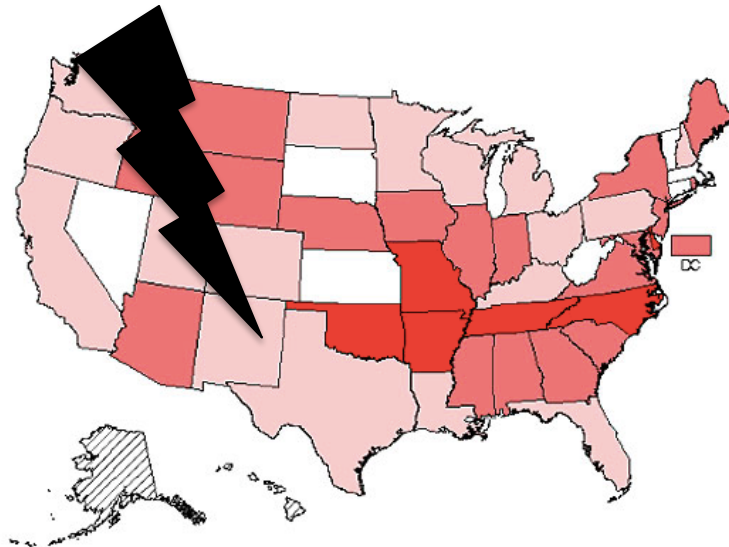


Tularaemia,  
tick paralysis



# *Rickettsia rickettsii*

- Rocky Mountain Spotted Fever
  - Not confined to the Rockies
- *Dermacentor variabilis* / *andersoni*



Cases per million



- Fever, headache
- Macular rash → petechial
- Eschar rare
- Mortality 30-80%

# Unusual clinical syndromes (1): SENLAT, TIBOLA, DEBONEL

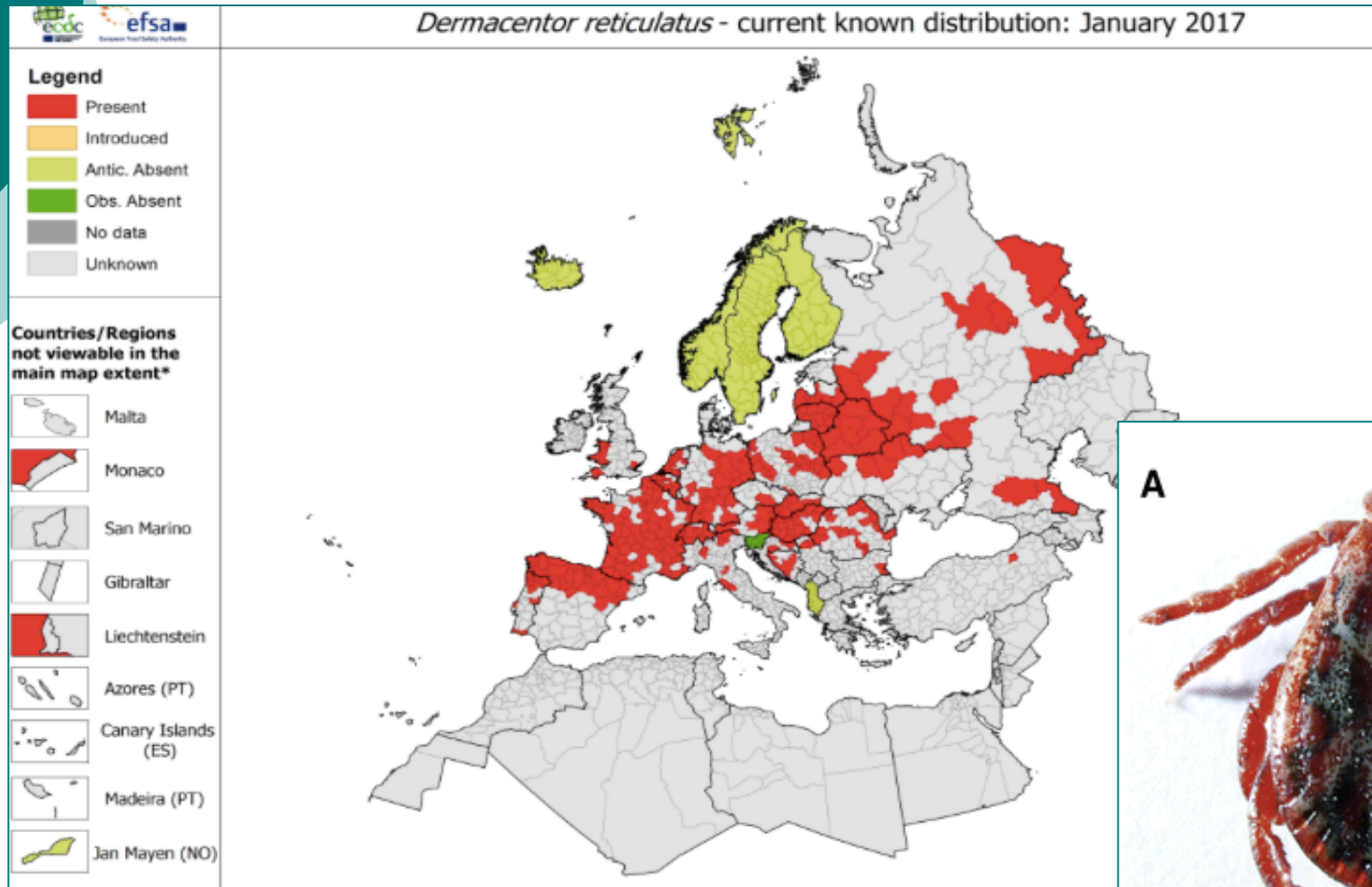
Mild



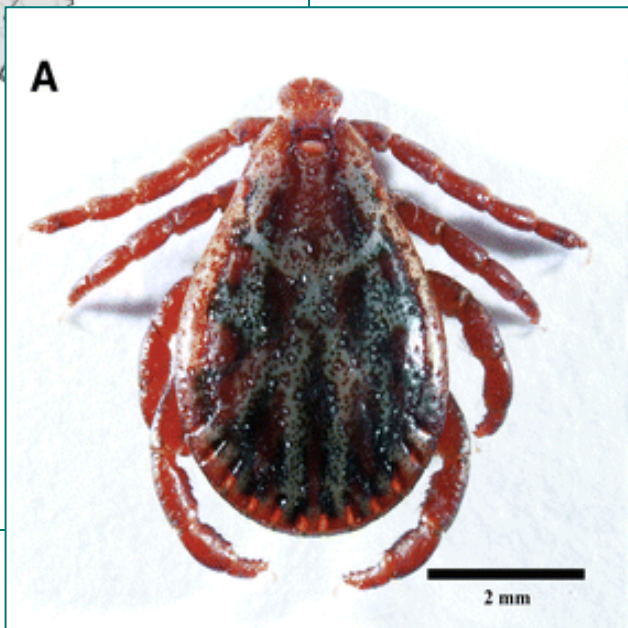
- Scalp Eschar and Neck Lymphadenopathy after Tick Bite
- *R. slovacae*
  - *D. marginatum* / *D. reticulatus*
- Central / Southern Europe
- May get residual alopecia and asthenia at site

# Unusual clinical syndromes (1): SENLAT

Mild



TBE, OHF



## Unusual clinical syndromes (2): lymphangitis associated rickettsiosis

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**Moderate**



- *R. sibirica* subsp. *mongolotimonae*
- France, Greece, Portugal, South Africa
- Fever, maculopapular rash
- One or more eschar
- Enlarged regional lymph nodes or lymphangitis
- Rarely severe illness

## Unusual clinical syndromes (3): Rickettsial pox



- *Rickettsia akari*
  - *Liponyssoides sanguineus*
- Probably a worldwide distribution
- Mouse extermination
- Painless red papule → vesicular → eschar
- Generalised rash
- Fever
- Regional lymphadenopathy

## The up and coming Rickettsia: *Rickettsia felis*

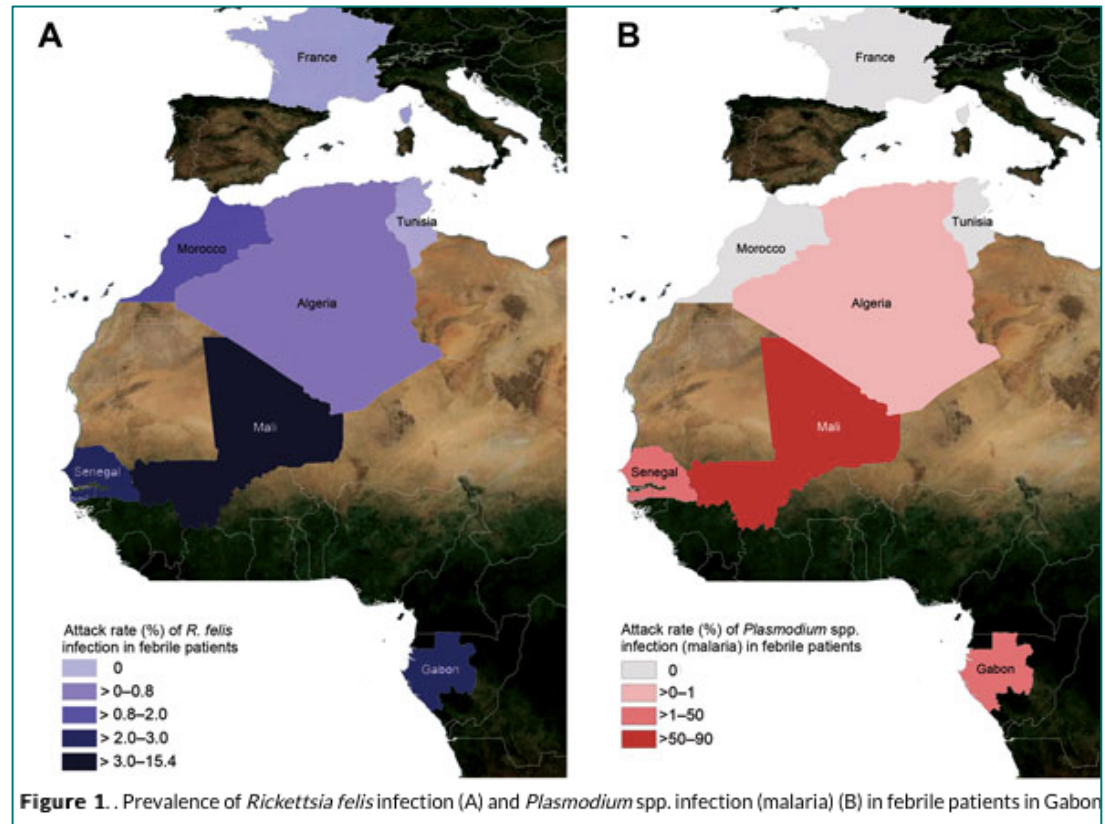
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- Unusual rickettsial pathogen
- Africa, Asia, Europe, North America
- Vector:
  - *Ctenocephalides felis*
  - *An. gambiae*
  - ? others
- Fever, headache, myalgia, rash
  - Occasional severe manifestations

?? Mild

# The up and coming Rickettsia: *Rickettsia felis*

- Senegal
  - 2024 patients with fever
  - 15% PCR +
  - 23% Pf patients had Rf.
- Mali, Gabon
  - 3 -10% febrile patients PCR positive
- Healthy people also PCR positive!



# Terminology: 3 groups

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- Spotted fever

- African spotted fever
- Mediterranean spotted fever
- Rocky mountain spotted fever
- + many more

- **Scrub typhus**

- Typhus group

- Epidemic typhus
- (Endemic)  
Murine typhus

Severe

# Scrub typhus

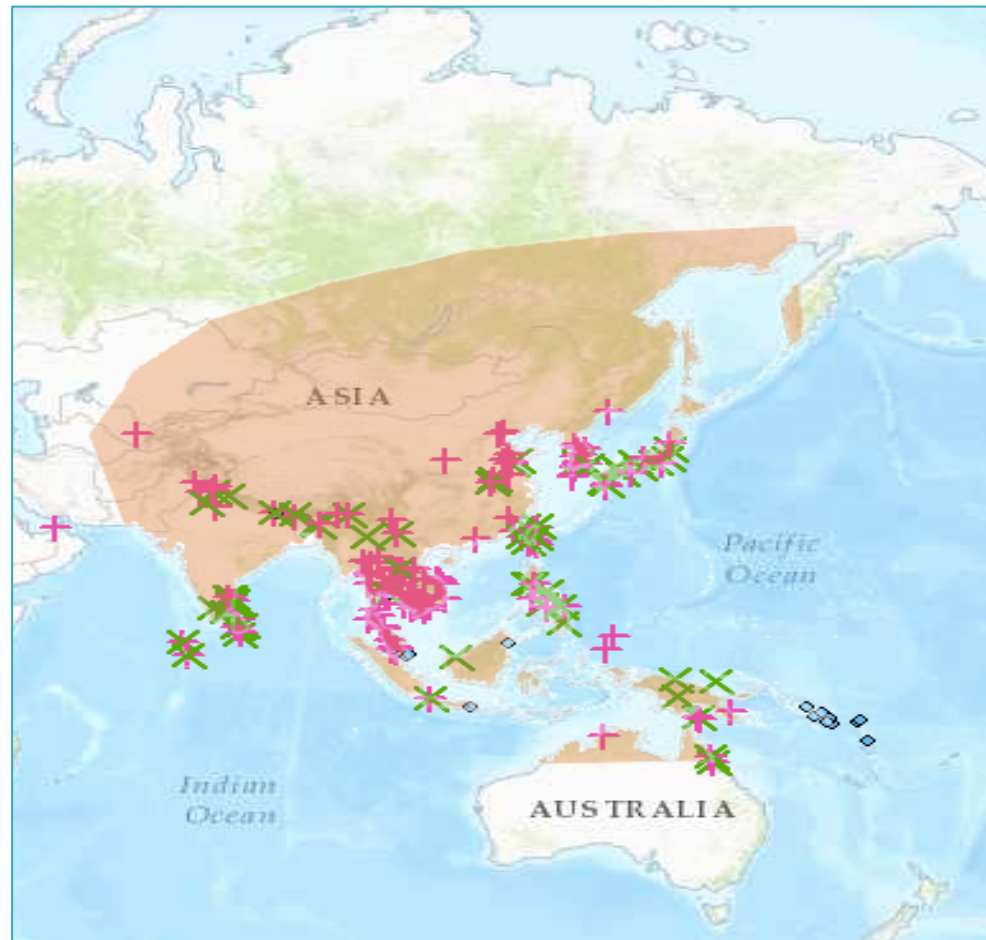
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- *Orientia tsutsugamushi*
- Larval stages of trombiculid mite  
“chiggers”
- Small mammal reservoir
- Symptoms
  - Fever, headache, myalgia
  - Eschar
  - Rash
- Complications
  - Meningoencephalitis, myocarditis, AKI
  - Sensorineural deafness



Mortality rate <25%

# Scrub typhus



Vector map: scrub typhus case mapping  
Walter Reed Biosystematics Unit at the Smithsonian Institute

# Terminology: 3 groups

---

- Spotted fever

- African spotted fever
- Mediterranean spotted fever
- Rocky mountain spotted fever
- + many more

- Scrub typhus

- **Typhus group**

- **Epidemic typhus**
- **(Endemic) Murine typhus**

**Severe**

# Epidemic typhus

- *R. prowazekii*
- Human body louse / *Pediculus humanus*
  - Crowded, unhygienic conditions
  - Transmitted by faeces
- Fever, headache, myalgia, rash
- Meningoencephalitis, myocarditis, splenomegaly

**CONTEXT****Mortality  
20-80%**

## Endemic typhus/ Murine typhus

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- *R. typhi*
- Oriental rat flea, *Xenopsylla cheopis*
- Transmitted by faeces
- Worldwide distribution
- Clinical
  - Fever, headache, myalgia, rash
  - No eschar
- Difficult to distinguish from spotted fevers

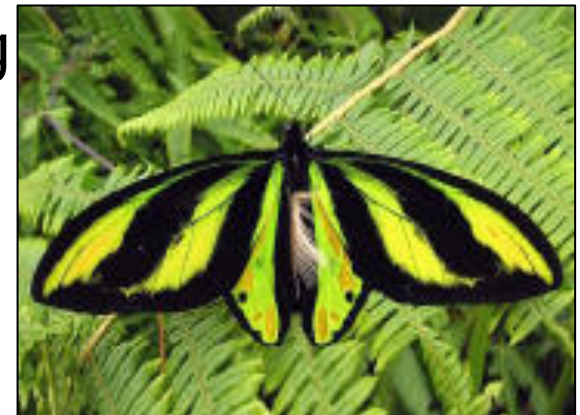


**Mortality 1-2%**

# Butterflies in West Papua

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- 55 year old M
- Previously fit and well
- West Papua
  - Jungle
  - Mud wading but no swimming
  - Photography
- 5 days after return
  - Fever, tired, headache



# Butterflies in West Papua

- D3 illness-GP ? Viral
- D5 illness- A+E
  - 40C, HR 110,
  - RR 16, 97% OA
  - Diffuse maculopapular rash

**Differential  
diagnosis?**

| Bloods      | Day 5      |
|-------------|------------|
| WCC         | 7          |
| Plt         | <b>80</b>  |
| Creat       | 88         |
| ALT         | 38         |
| ALP         | 110        |
| Albumin     | <b>32</b>  |
| CRP         | <b>262</b> |
| Malaria RDT | Neg        |

# Butterflies in West Papua

- D8 illness
  - 39C
  - Rash improving
  - Worsening shortness of breath
    - PO2 9 on air

| Bloods       | Day 5      | Day 8      |
|--------------|------------|------------|
| WCC          | 7          | 6          |
| Plt          | <b>80</b>  | <b>52</b>  |
| Creat        | 88         | 93         |
| ALT          | 38         | <b>196</b> |
| ALP          | 110        | <b>245</b> |
| Albumin      | <b>32</b>  | <b>23</b>  |
| CRP          | <b>262</b> | <b>296</b> |
| Malaria RDT  | Neg        | Neg        |
| Malaria film | Neg        | Neg        |

**Treatment?**

# Butterflies in West Papua

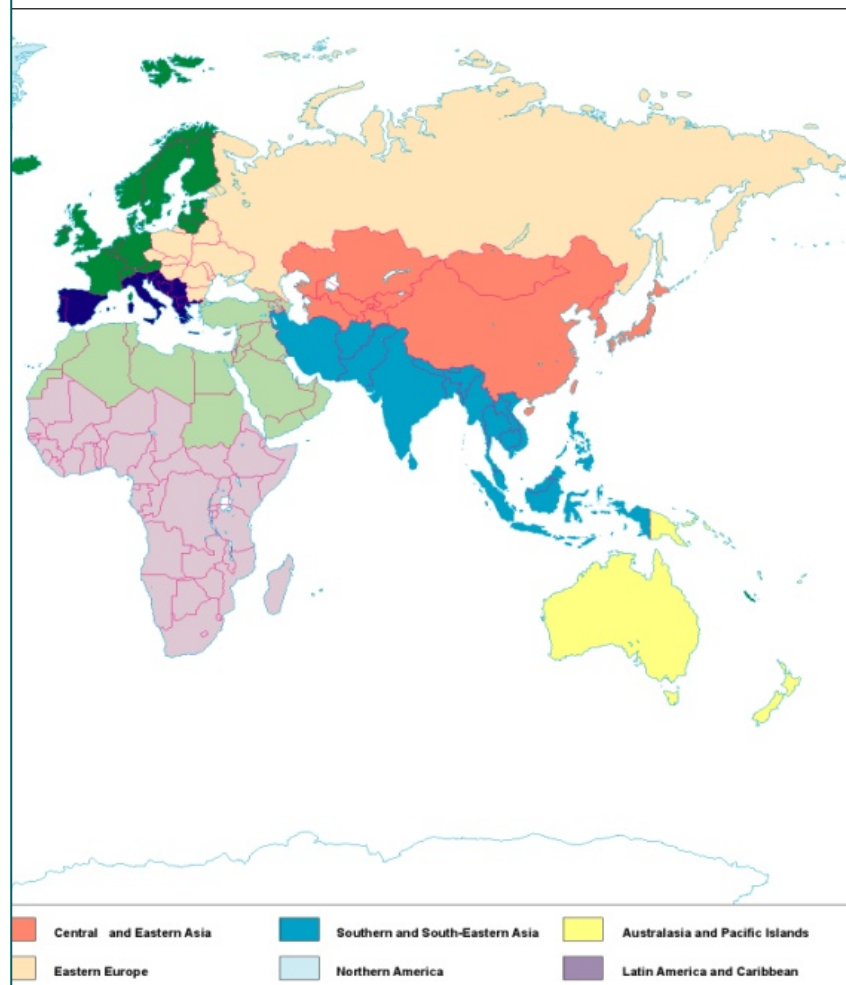
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- Increasingly sick
- Dengue PCR and IgM negative
- Started ceftriaxone and doxy
- Further serum sent for geographical screen

Why does this not fit with dengue?

# Southern and SE Asia Panel

- Flaviviruses – dengue, West Nile, TBE, JE
- Alphaviruses - Chikungunya
- Sandfly fever viruses
- Rickettsia- SF/ET IgM/G
- Scrub Typhus
- Leptospirosis



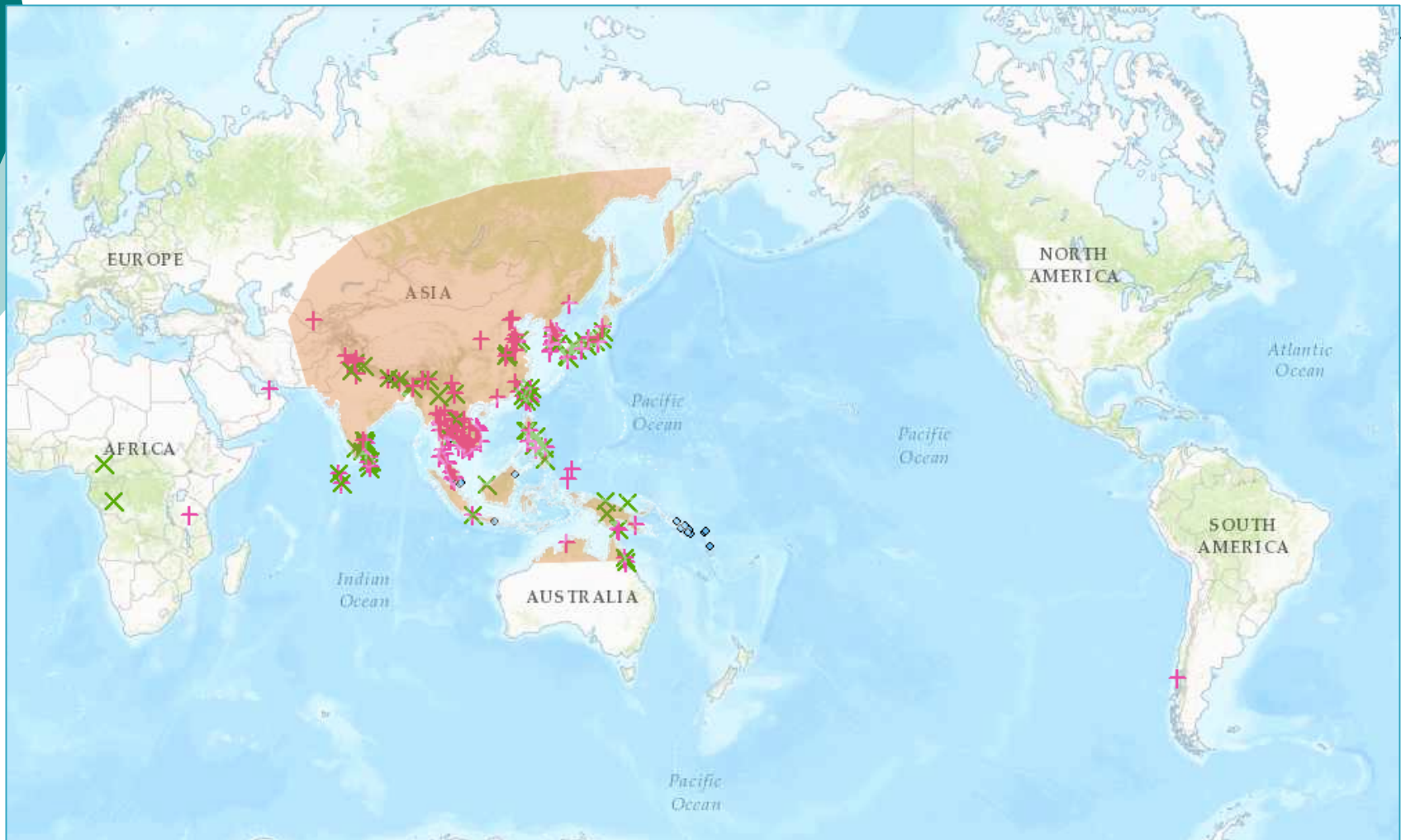
# Butterflies in West Papua

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- Defervesced within 48 hours
- Discharged home

Scrub typhus IgM and  
IgG positive

# Scrub typhus

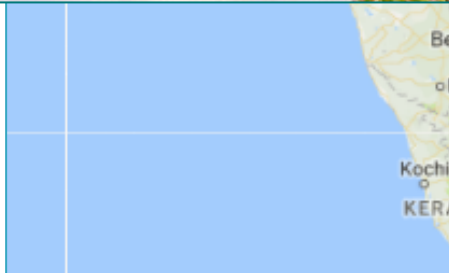


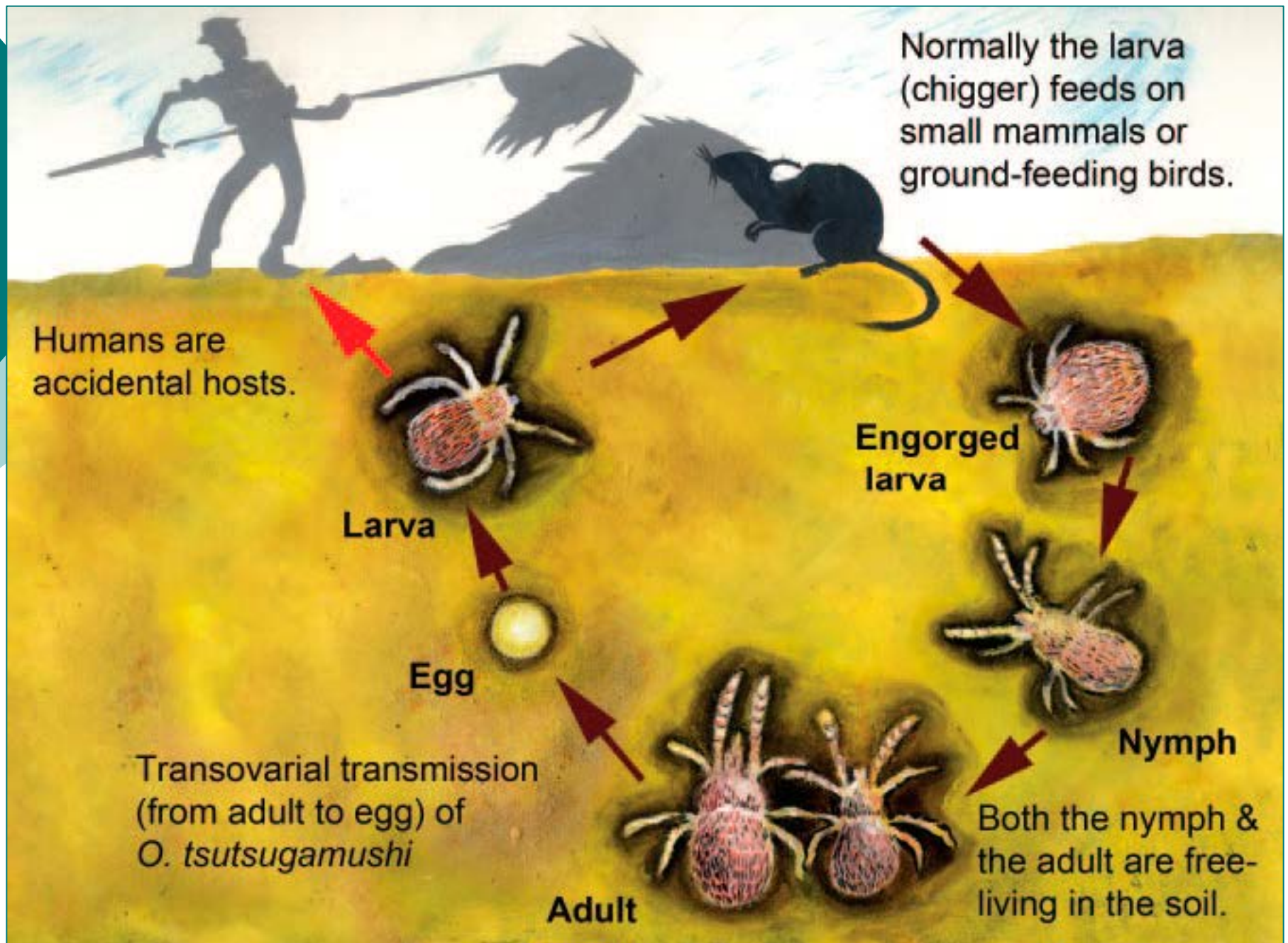
Vector map: scrub typhus case mapping  
Walter Reed Biosystematics Unit at the Smithsonian Institute

Studies India

Sikkim

- 36% scrub
- tongue
- aria
- eric



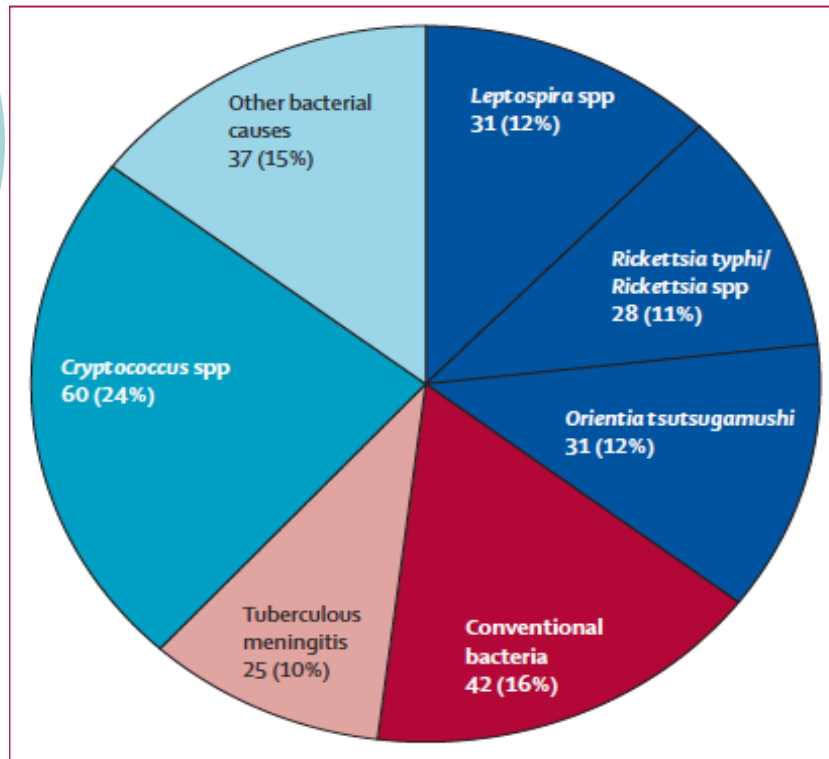


# Scrub typhus - India

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- 55% eschar
    - 66% headache
    - 60% SOB
  - Severe disease
    - ARDS – 43%
    - Jaundice- 25%
    - Aseptic meningitis- 20%
    - AKI – 13%
    - MOF – 38%
  - Mortality 1-8%
  - Immunity short lived and strain specific
- Difficult to distinguish from severe dengue
    - Subtleties- WCC, PLT, LFTs, altered sensorium

# Scrub typhus



**Figure 1: Summary of diagnosed bacterial and fungal infections**

Conventional bacteria were defined as *Streptococcus pneumoniae*, *Neisseria meningitidis*, *Haemophilus influenzae*, or *S suis*.

- CSF
  - WCC 80
    - 2/3 WCC <100
    - 10% > 200
  - Mostly lymphocytes
- Mildly elevated protein, usually <1
- Normal glucose

Dittrich et al Lancet Global Health 2015 3:e104-112

Varghese et al. Differential diagnosis of scrub typhus from bacterial meningitis using clinical and laboratory features. Neurology India. 2013

# Butterflies in West Papua

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- Scrub typhus is very common
- It can be difficult to distinguish clinically from dengue
  - Look carefully for the eschar
  - Subtleties- WCC, Hb, low sats, altered sensorium
- If in doubt, give doxycycline
- Always send a geographical panel and convalescent serology
  - It costs the same amount but you get MUCH more information

# The young explorer

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- 10 year old F
  - 2/52 trip to Australia
- Northern Queensland
  - national parks
- Small cut on foot
  - infected -7 days flucloxacillin
- 7 days after return
  - fever
  - abdominal pain
  - maculopapular rash



# The young explorer

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○ rash

- Bloods
  - WCC 5.6, LCY 0.8
  - PLT 107
  - Creat 65
  - ALT 16

# The young explorer

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## Differential diagnosis?

### Australian pathogens

- scrub typhus
- melioid
- spotted fever

### Others

- community acquired
  - pneumococcal
  - meningococcal
- measles

## The young explorer

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- Admitted started ceftriaxone
- Hypotensive, tachycardic, increasing BE
- Increasing size of spleen
- CRP 165 → 300

No improvement

Switched to meropenem and doxycycline

# The young explorer

- Negative blood and urine culture
- Worsening chest xray- ARDS

What infections are excluded?

- Dengue
- Chikungunya
- Ross River
- Japanese encephalitis
- Murray Valley

| Infection             | PCR | IgM | IgG |
|-----------------------|-----|-----|-----|
| Dengue                | —   | —   | —   |
| Murray Valley         |     |     | —   |
| Japanese encephalitis |     | —   | —   |
| Chikungunya           |     | —   | —   |
| Ross River            |     | —   | —   |
| Epidemic typhus       |     | —   | —   |
| Spotted fever         |     | —   | —   |
| Scrub                 | —   | —   | —   |
| Leptospirosis         | —   | —   | —   |
| Coxiella              |     | —   | —   |
| Melioid               | —   |     |     |

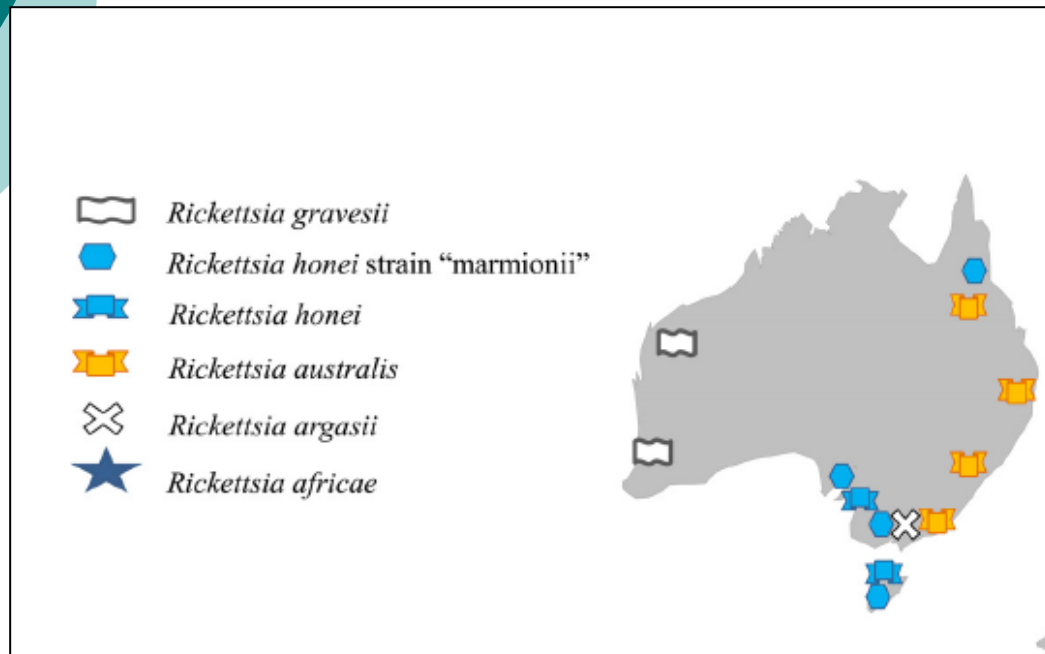
# The young explorer

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| Infection       | IgM | IgG  |
|-----------------|-----|------|
| Epidemic typhus | -   | 512  |
| Spotted fever   | -   | 1024 |
| Scrub           | -   | -    |
| Leptospirosis   | -   | -    |
| Coxiella (ph2)  | -   | -    |

**Queensland  
tick typhus/  
spotted fever**

# Australian rickettsial infections



- *R. australis*
  - Queensland
  - Macpap rash
  - Occasional severe disease
  - June-Nov
- *R. honei*
  - Victoria, SA
  - Petechial rash
  - Usually mild
  - Dec-Jan

# Conclusion

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- Rickettsial infections
  - Found worldwide- restricted geographical areas
  - Diagnosis modalities are similar for all
  - Most present with fever, myalgia, headache
    - +/- rash
    - +/- eschar
    - +/- variable signs of severity
      - vasculitic syndrome
      - CNS disease



# Conclusion

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- Consider rickettsia. You don't need to know which specific infection you are looking for!
- If in doubt
  - Give doxycycline
  - Send serology with convalescent sample 3 weeks later



# Acknowledgements

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Imported Fever Service Team

Kate Woods

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George Varghese and team,  
Christian Medical College, Vellore