

A Patient with Fever after a Trip to South-East Asia

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History & Physical Exam

- 38 year old Caucasian male
- 4 week bicycle trip as a tourist guide through rural areas of Thailand, Cambodia and Vietnam
- weakness and fever up to 40°C for five days with headache, neck stiffness, 3 episodes of diarrhea
- resident of Berlin, frequent travels to tropical countries as a guide
- no known preconditions, no medication
- physical exam: subtle, generalized, maculopapular rash, enanthema, subtle conjunctivitis

What diagnostic tests would you perform?

Laboratory results and further diagnostic tests

- hyponatremia: 129mmol/l (134-145)
- **thrombocytopenia**: 75/nl (150-400)
- infection/inflammation: CRP 77mg/l (<5)
- differential blood count with “left shift” (band cells↑) and **relative lymphocytopenia** of 18% (25-40)
- **elevated transaminases**: AST 276 U/l (<50) and ALT 235 U/l (10-40)
- within the normal limit: creatinine (UNL), procalcitonin, bilirubine, hemoglobin
- abdominal ultrasound: **splenomegaly**
- chest x-ray: **left lower lobe suggestive of pneumonia**
- unremarkable tests: ecg, urinalysis

Probable entity of infection: bacterial, viral, fungal, helminthic?

Differential diagnosis?

Laboratory results and further diagnostic tests

- hyponatremia
- thrombocytopenia
- infectious etiology
- differential lymphocyte count
- elevated liver enzymes
- within normal range
- hemoglobin
- abdominal pain
- chest pain
- unremarkable



relative

U/I (10-40)
tubine,

Probably

infectious?

Possible diagnoses?

- ~~Malaria~~ (2nd most frequent infectious disease worldwide after TB)
- ~~Dengue~~ (most frequent viral infection after travel to tropics)
- ~~Acute HIV infection~~
- **Leptospirosis** (inhaled urine of rodents, biphasic course, hepatitis, nephritis)
- ~~Salmonella typhi~~ (frequent, splenomegaly, obstipation → diarrhea)
- **Rickettsiosis** (tick-borne, thrombozytopenia, transaminases, rash, pulmonary complications)
- **Brucellosis** (domestic animals / livestock, hepatosplenomegaly)

Suspected diagnosis: **Leptospirosis**

Start of treatment with Ceftriaxone (i.v.) and Clarithromycin (p.o.)

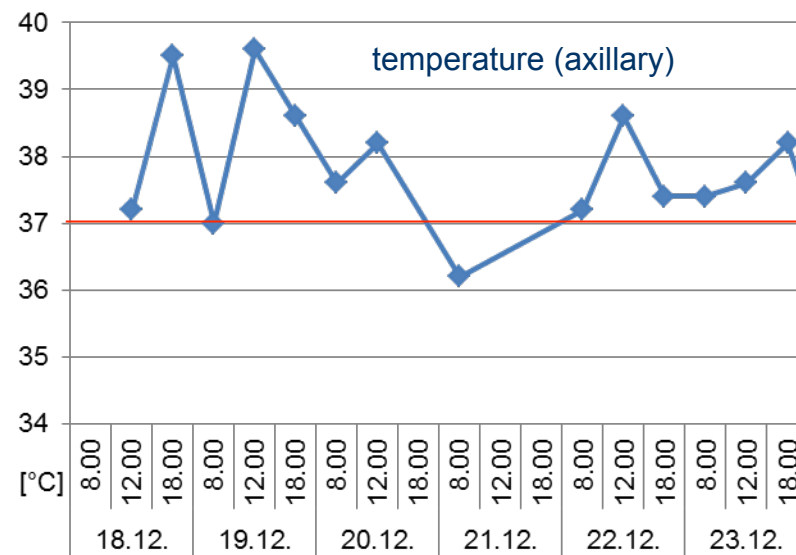
Serology

Brucella-Serologie		
Brucella-IgG-AK (EIA)	negativ	U/ml
Brucella-IgM-AK (EIA)	negativ	
Leptospira-Serologie		
Leptospiren-IgG (EIA)	negativ	U/ml
Leptospiren-IgM (EIA)	negativ	< 15
Rickettsia-Serologie		
R.rickettsi IgG°	1:64	Titer
Referenzbereich :	< 1:64	
R.rickettsi IgM°	< 1:64	Titer
Referenzbereich :	< 1:64	

Stool samples 2x negative for parasites, worms, shigella, salmonella, campylobacter, yersinia

What is the restriction of serology tests?

Course of Disease

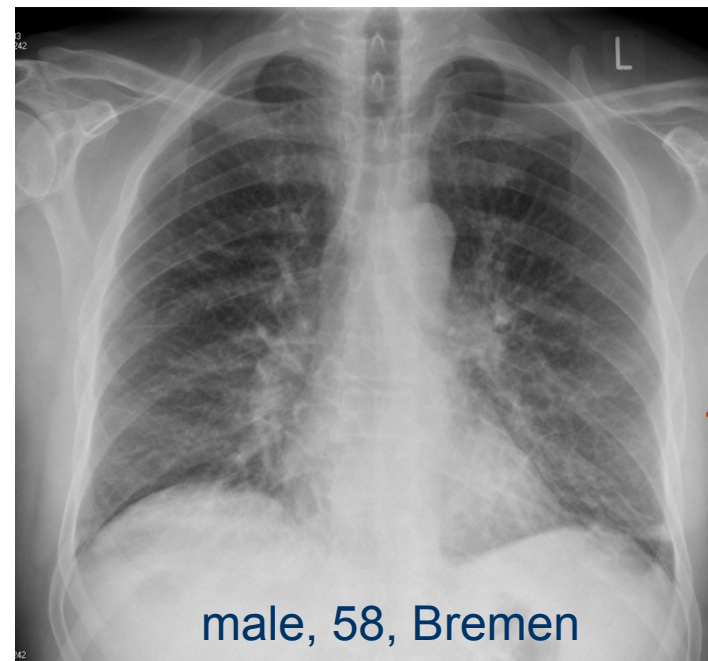
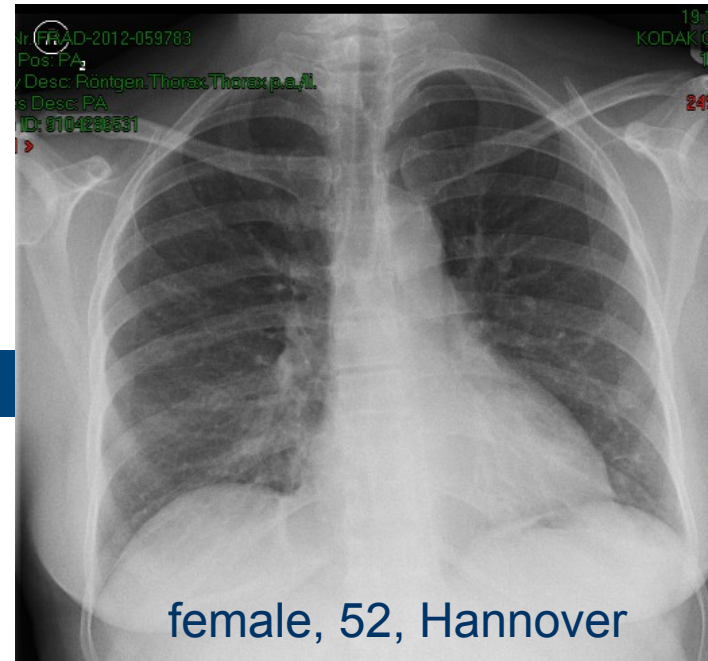


Further Patients

- fever, rash
- **thrombozytopenia**
- elevated CRP
- **relative lymphozytopenia**
- **elevated transaminases**
- splenomegaly
- suspected pneumonia

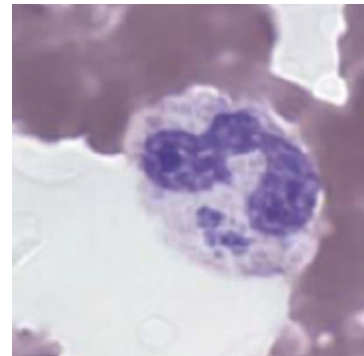
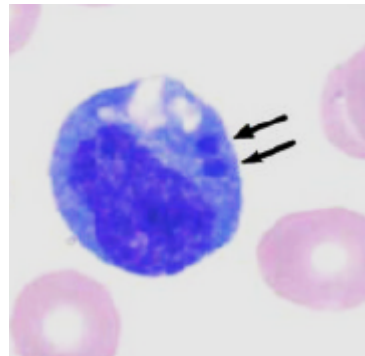
- negative microbiology / serology

- Levofloxacin/Ceftriaxone
- Clarithromycin



New Results

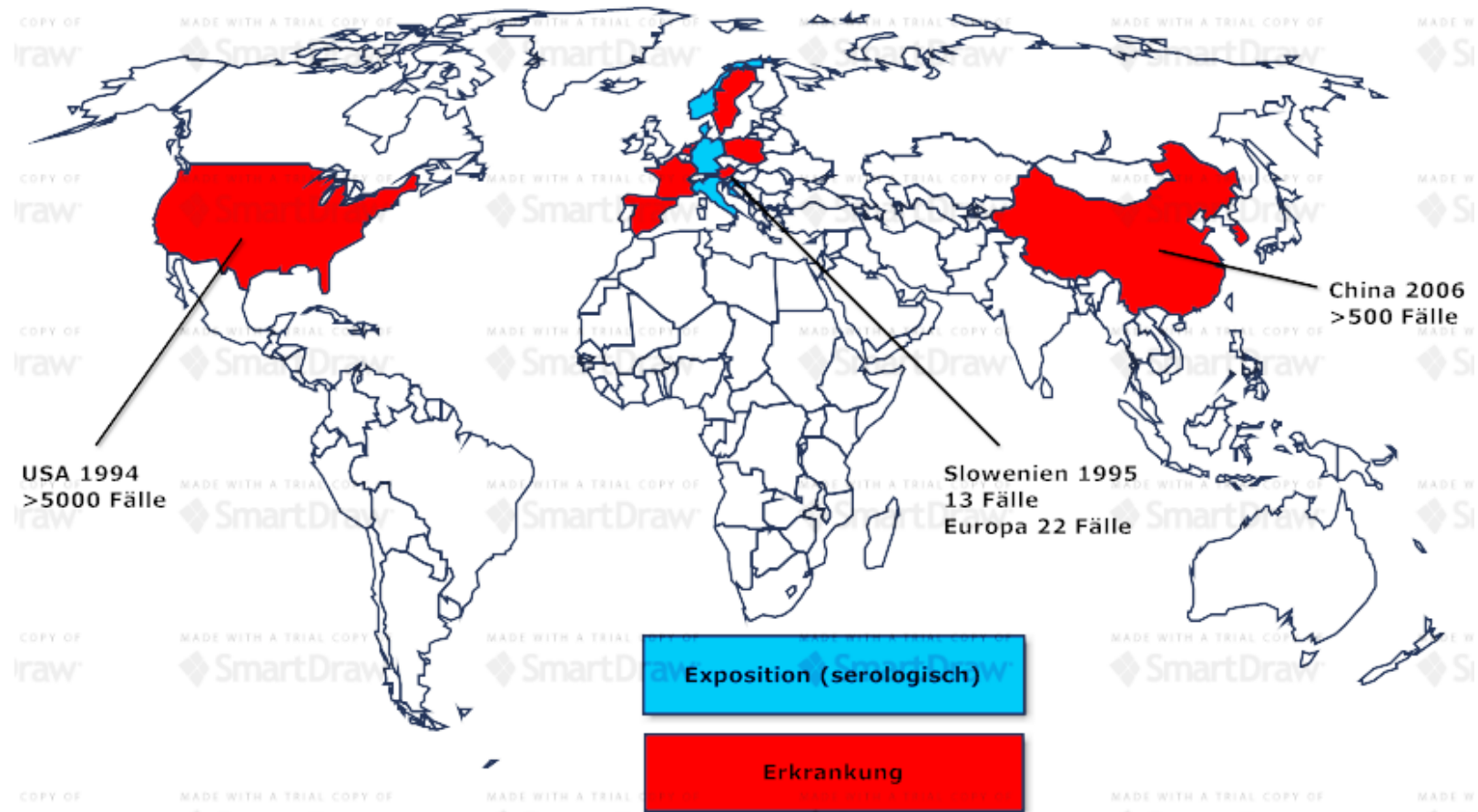
- Laboratory reports: vacuoles / morulae in monocytes and neutrophils



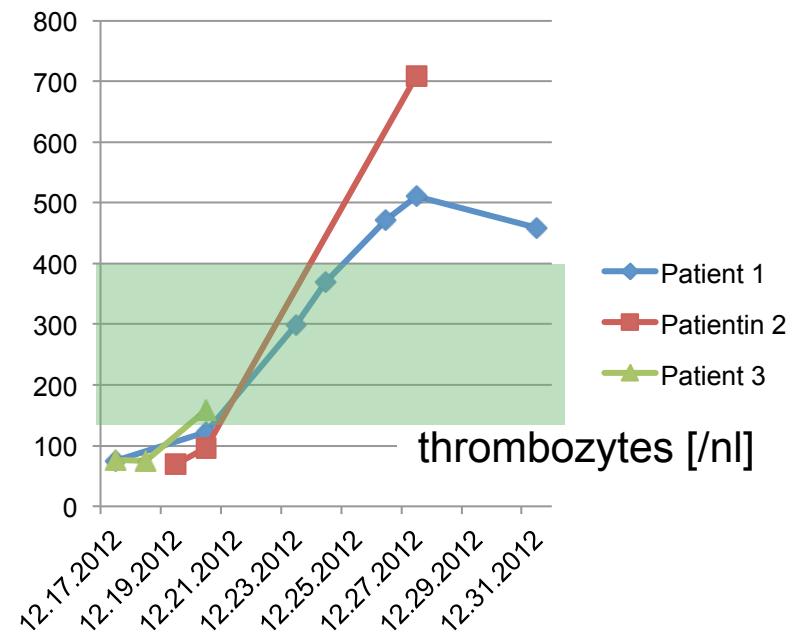
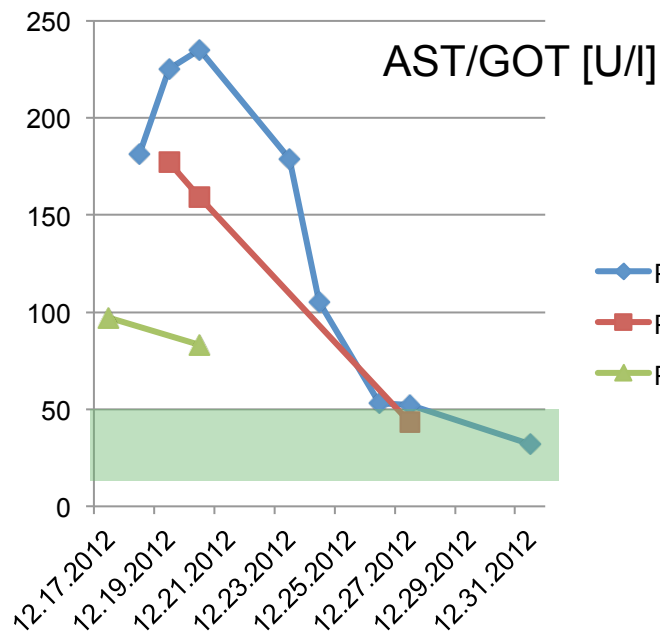
Ismael et al., Human Ehrlichiosis and Anaplasmosis, Clin Lab Med 2010

New suspected diagnosis: “Ehrlichiosis”

„Ehrlichiosis“



Course of Disease - Overview



Final Results

Patient 1 (Berlin):

	18.12.12	29.12.12	30.01.13
Anaplasma phagocytophilum IgG-antibody	1:128 positive	1:256 positive	1:64 positive
Anaplasma phagocytophilum IgM-antibody	negative	1:40 positive	negative
A. phagocytophilum PCR	positive	-	negative

Patient 2 (Hannover): no samples received

Patient 3 (Bremen):

	28.01.13
Anaplasma phagocytophilum IgG-Antikörper	<1:64 negative
Anaplasma phagocytophilum IgM-Antikörper	1:80 positive

Threshold:

IgM 1:20

IgG 1:64

Final Diagnosis



Human granulocytic anaplasmosis
(HGA)

THANK YOU FOR YOUR
ATTENTION!

Appendix - I

อ่าวไทย

Am Golf von Thailand

Radtour von Bangkok nach Saigon
Vom 17. November bis 16. Dezember 2012

Vorläufiges Programm (Abweichungen möglich!)

Sa . 17.11. (1. Tag)

11:05 Uhr Abflug in Frankfurt (QR28), 19:05 Uhr
Ankunft in Doha. 20:45 Uhr Weiterflug nach Bangkok
(QR612).

So . 18.11. (2. Tag)

07:00 Uhr Ankunft in Bangkok, Transfer in Hotel.
Sightseeing

Mo . 19.11. (3. Tag)

Kleine Stadtrundfahrt mit dem Rad,

Strecke: 120km

Mo . 03.12. (17. Tag)

Tagesausflug im Kirirom-Nationalpark
Strecke: ca. 60km

Di . 04.12. (18. Tag)

Kirirom – Kampot
Strecke: ca. 100km

Mi . 05.12. (19. Tag)

Tagesausflug zum Bokor Mountain
Strecke: ca. 50km

Appendix - II

	A. phagocytophilum		E. chaffeensis		N. sennetsu	
	in vitro	in vivo	in vitro	in vivo	in vitro	in vivo
Doxycyclin	S		S		S	
Tetracyclin						S
Rifampicin	S		S		S	
Ciprofloxacin	bakteriost.		R		S	
Trovaflaxacin	S					
Levofloxacin	S					
Ofloxacin	S					
Erythromycin	R		R		R	R
Azithromycin	R					
Gentamicin			R			
Clindamycin	R					
Penicillin			R		R	R
Cotrim	R		R		R	
Chloramphenicol	bakteriost.		R		R	R

There is no published experience about the use of clarithromycin, azithromycin, ciprofloxacin or recently released fluoroquinolones for treatment of **human** granulocytotropic anaplasmosis.

Appendix - III: Taxonomy

ORDER	FAMILY	GENUS	SPECIES
Rickettsiales	Anaplasmataceae	Anaplasma	A. phagocytophilum (<i>Ehrlichia phagocytophila</i>)
		Ehrlichia	E. chaffeensis, E. ewengii
		Neorickettsia	N. Sennetsu (<i>Rickettsia</i> oder <i>Ehrlichia sennetsu</i>)
	Rickettsiaceae Rickettsia typhi / rickettsii ...