

Fever in the Returned Traveler

with a focus on Africa

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Outline

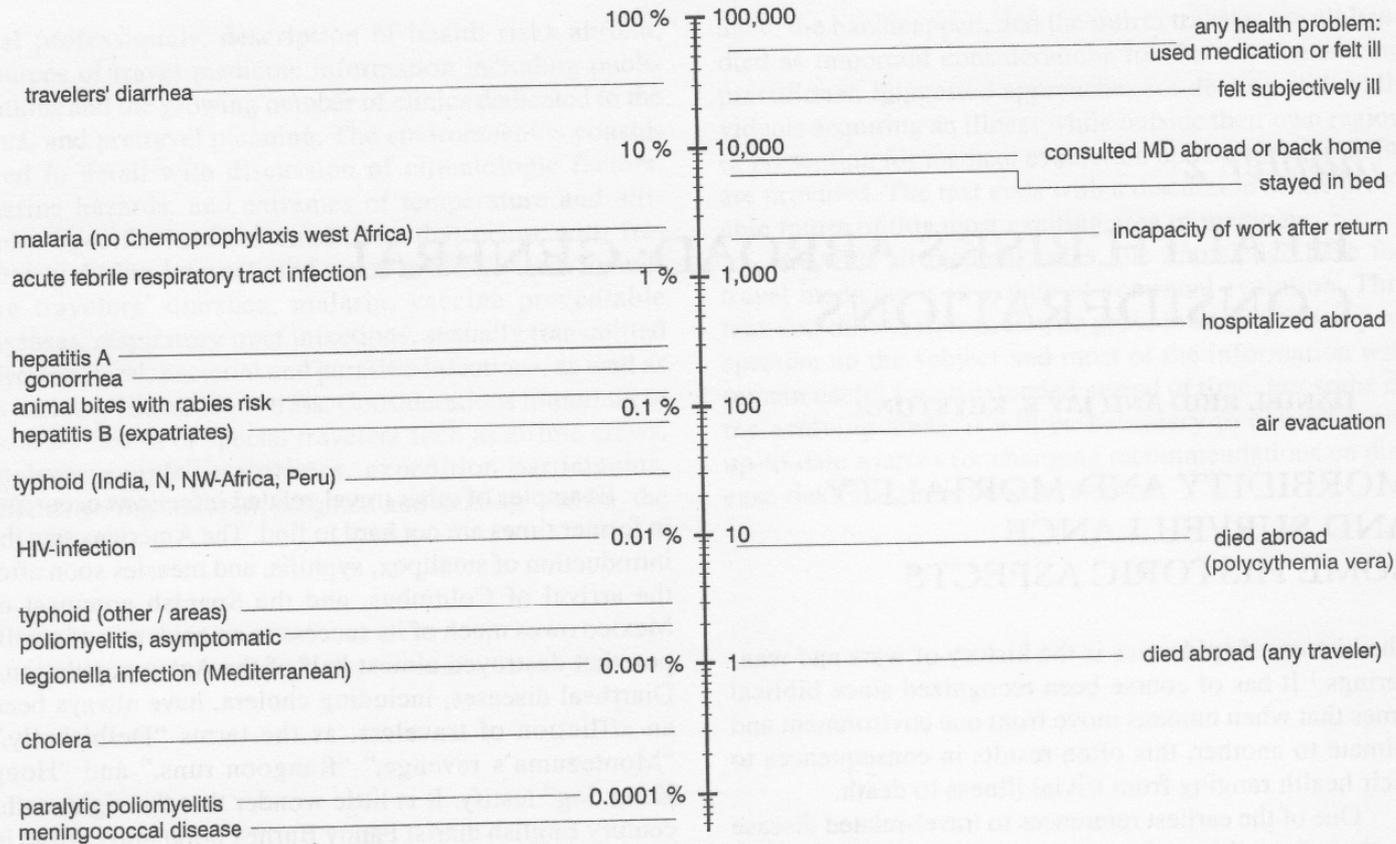
- Introduction
- Epidemiology of illness in the returned traveler
- General assumptions
- Clinical scenarios
- Specific pathogens of interest
- Sources of information
- Final comments

Caveats about your speaker

- He's clinically trained but not an operational type.
- He's in the PHS, for God's sake.
- He's assigned to a University, but don't confuse him with an academician.

Outline

- Introduction
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Incidence rate per month of health problems during a stay in developing countries

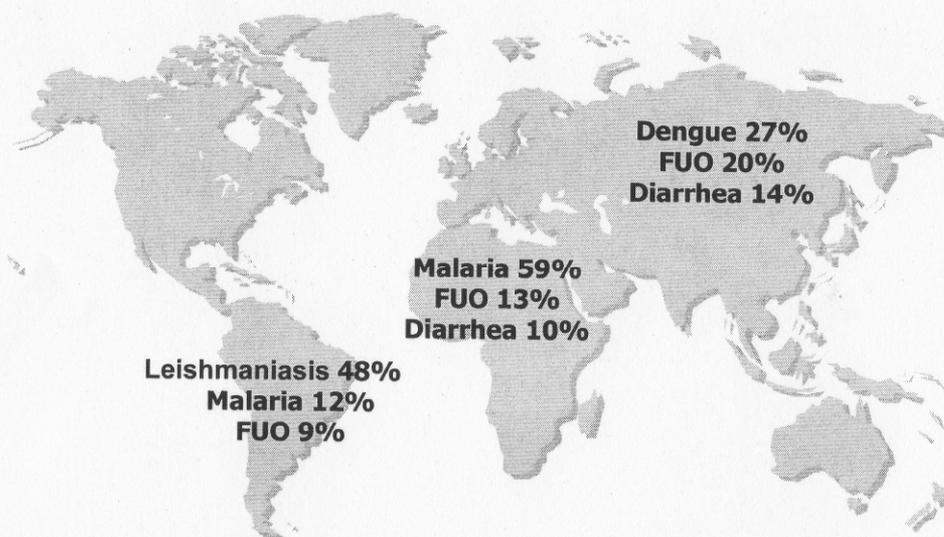


Figure 1 Diseases and destinations: the three most common diagnoses in each continent visited. FUO = fever of unknown origin

Table 1 Distribution of Main Diagnoses Leading to Post-travel Hospitalization*

Disease	No. of Patients (% of Total Cases)	
	Febrile	Nonfebrile
Malaria	54 (26)	None
Unidentified febrile diseases	34 (16)	None
Dengue fever	27 (13)	None
Diarrheal diseases	14 (7)	10 (4)
Leishmaniasis	None	18 (9)
Miscellaneous febrile infections	12 (6) [†]	None
Skin diseases	7 (3) [‡]	4 (2) [§]
Pneumonia	7 (3)	None
Noninfectious diseases	None	7 (3)
Onchocerciasis	None	5 (2)
Idiopathic eosinophilia	None	4 (2)
Hepatitis infectious	4 (2)	None
Pulmonary schistosomiasis	2 (1)	None
Amebic liver abscess	2 (1)	None

*N = 211.

[†]Epstein-Barr virus (3), leptospirosis (2), echinococcal abscess (1), infective endocarditis (1), viral meningitis (1), upper respiratory tract infection (1), rubella (1), cat-scratch disease (1), tonsillitis (1).

[‡]Infected wounds (3), cellulitis (2), erysipelas (2).

[§]Infected myiasis (2), nonspecific rash (1), urticaria (1).

^{||}Anxiety (2), dizziness (1), hemolytic anemia (1), mefloquine adverse effect (1), hematologic malignancy (1), myositis (1).



GeoSentinel

The Global Surveillance Network
of the ISTM and CDC

a worldwide communications & data collection
network of travel/tropical medicine clinics

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2 NEW GeoSentinel PUBLICATIONS:

"Illness in Children After International Travel: Analysis from the GeoSentinel Surveillance Network"

Pediatrics. Published online April 5, 2010.

[click here to download PDF \(596kB\) of this article](#)

"Sex and Gender Differences in Travel-associated Disease"

Clin Infect Dis. 2010 Mar;50(6):826-32.

[click here to download PDF \(321kB\) of this article](#)

GeoSentinel is a worldwide communication and data collection network for the surveillance of travel related morbidity. It was initiated in 1995 by the International Society of Travel Medicine (ISTM) and the Centers for Disease Control (CDC) as a network of ISTM member travel/tropical medicine clinics. GeoSentinel is based on the concept that these clinics are ideally situated to effectively detect geographic and temporal trends in morbidity among travelers, immigrants and refugees.

Current activities include:

GeoSentinel Surveillance Sites

GeoSentinel Sites participate in **surveillance and monitoring of all travel related illnesses** seen in their clinics. Aggregation of this data across the network of 49 globally dispersed medicine clinics on all continents (15 in the United States and 34 in other countries) allows linking of final diagnoses in migrating populations with similar geographic exposures. In addition to formal surveillance, GeoSentinel sites also participate in enhanced surveillance and networking with public health partners.

[Information on becoming a GeoSentinel Site](#)

[GeoSentinel Data Entry \(Sites Only\)](#)

GeoSentinel Network Members

GeoSentinel Network Members are ISTM provider clinics that **informally provide leads and contacts** when they encounter any patient having a pre-defined alarming diagnosis or unusual event. Network Members also participate in brief e-mail queries for enhanced surveillance and response in potential outbreak situations. This program allows large numbers of individual members in many countries to be rapidly linked together to share clinical observations and facilitates direct interaction with health authorities.

[Information on becoming a GeoSentinel Network Member](#)

[GeoSentinel Network Members Only](#)

Table 2. Diagnosis According to Syndrome Group and Travel Region among Ill Travelers Returning from the Developing World.*

Diagnosis	All Regions (N=17,353)	Caribbean (N=1115)	Central America (N=1326)	South America (N=1675)	Sub-Saharan Africa (N=4514)	South Central Asia (N=2403)	Southeast Asia (N=2795)	Other or Multiple Regions (N=3517)†
Systemic febrile illness‡	226	166	153	143	371	171	248	145
Acute diarrhea‡	222	196	234	219	167	327	210	238
Dermatologic disorder‡	170	261	255	264	127	130	212	125
Chronic diarrhea‡	113	133	133	130	57	129	97	149
Noninfectious gastrointestinal disorder‡	82	87	75	82	70	74	58	121
Respiratory disorder‡	77	48	49	50	77	89	97	86
Nonspecific symptoms or signs‡	70	53	51	59	75	85	63	77
Genitourinary disorder‡	35	29	11	27	51	25	29	40
Asymptomatic parasitic infection‡	30	18	26	33	29	44	30	24
Underlying chronic disease‡	19	14	13	18	20	14	13	27
Injury‡	14	23	11	14	7	15	14	21
Neurologic disorder‡	15	23	24	16	10	15	10	16
Adverse drug or vaccine reaction‡	12	4	5	5	26	12	8	8
Psychological disorder‡	12	8	20	15	8	12	10	18
Tissue parasite‡	10	5	5	11	22	4	3	7
Cardiovascular disorder	8	12	7	5	8	7	5	10
Obstetrical or gynecologic disorder	3	1	2	2	4	3	3	3
Ophthalmologic disorder	2	2	2	2	2	1	1	2
Dental problem	1	1	1	1	1	0	2	1
Death	1	1	0	0	1	3	0	1
Loss to follow-up‡	8	9	12	9	8	5	4	13

*Diagnoses included in each syndrome category are listed in the Supplementary Appendix. Numbers may not total 1000 because patients may have had more than one diagnosis.

†This category includes travel to West Asia, Northeast Asia, eastern Europe, Oceania, North Africa, or Antarctica (1868 travelers) or to multiple developing regions, for which ascertainment of exposure was impossible (1549 travelers).

‡P<0.01 for the comparison among regions.

Freedman, D.O., et al. Spectrum of Disease and Relation to Place of Exposure among Ill Returned Travelers. NEJM 2006; 354: 119-30.

Table 3. Etiologic Diagnoses within Selected Syndrome Groups, According to Travel Region.*

Syndrome and Cause	All Regions	Caribbean	Central America	South America	Sub-Saharan Africa	South Central Asia	Southeast Asia	Other or Multiple Regions†
Systemic febrile illness (n=3907)								
Specific pathogen or cause reported‡	594	459	527	446	718	522	547	454
Malaria‡	352	65	133	133	622	139	130	234
Dengue‡	104	238	123	138	7	142	315	35
Nonnucleosidic (due to Epstein-Barr virus or cytomegalovirus)‡	32	70	69	79	30	17	32	63
Rickettsial infection‡	31	0	0	0	56	10	16	24
Salmonella typhi or S. paratyphi infection‡	20	22	25	17	7	141	26	24
No specific cause reported‡	405	541	473	554	282	478	453	546
Acute diarrhea (n=3859)								
Parasitic diarrhea‡	354	383	403	368	353	453	262	323
Giardiasis‡	173	132	136	158	177	286	118	132
Amebiasis‡	120	105	155	142	138	103	74	135
Presumptive parasitic cause‡	35	9	45	52	33	55	33	13
Bacterial diarrhea‡	263	360	190	353	250	294	349	227
Campylobacter infection‡	85	46	32	90	73	87	130	57
Shigella infection	41	37	26	41	46	61	26	34
Nontyphoidal salmonella infection‡	27	27	13	14	29	12	56	30
Presumptive bacterial cause	110	132	94	106	99	136	116	95
Viral diarrhea‡	0	23	32	5	7	4	5	7
Unspecified acute diarrhea‡	385	457	377	376	357	289	393	451

Freedman, D.O., et al. Spectrum of Disease and Relation to Place of Exposure among Ill Returned Travelers. NEJM 2006; 354: 119-30.

24,920 returnees

March 1997 – March 2006

6957 (28%) with CC of fever

2559 (37%) from SSA

Sites include:

USA/Canada (25%)

Europe (53%)

Israel (9%)

Aus/NA (8%)

Asia (5%)

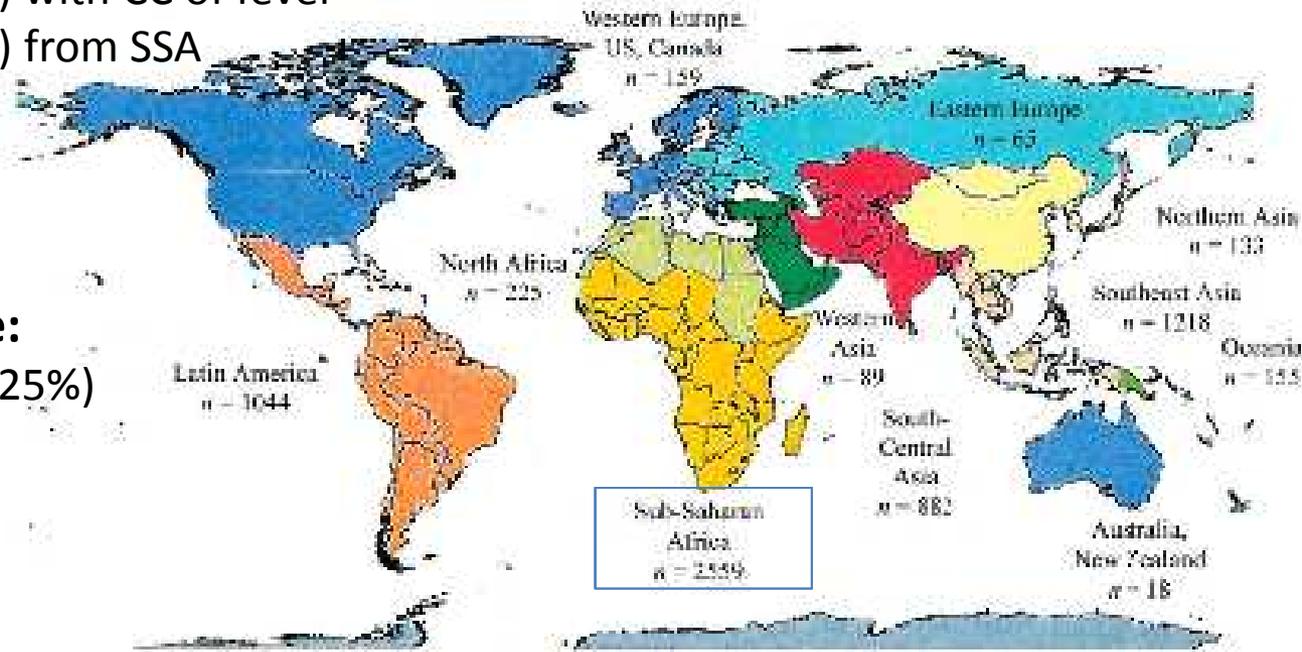


Figure 1. Distribution of regions of the world visited by ill travelers. A total of 5957 patients experienced fever; information regarding region of travel was missing or travel was to multiple regions for 403 travelers.

From Wilson, M., et al. Fever in Returned Travelers: Results from the GeoSentinel Surveillance Network. Clin Infect Dis 2007; 44: 1560-8

Table 1. Characteristics of returned ill travelers with and without fever (6957 patients with fever among 21,920 ill returned travelers).

Characteristic	No. (%) of ill returned travelers with fever	No. of ill returned travelers without fever	Regional multiple logistic regression models in which variable is included as a significant ^a predictor
Age, years			
<20	429 (31)	962	NS
20-64 ^b	6230 (88)	16152	—
≥65	244 (4)	761	NS
Sex			
Male ^b	3995 (57)	6662	—
Female	2991 (43)	6962	A, B, C, D
Reason for travel			
Tourism ^b	3802 (55)	10762	—
Business	1036 (15)	2477	—
Research/education	283 (4)	785	—
Missionary/volunteer	384 (5)	1734	B, C
Visiting friends and relatives	1431 (21)	2109	A, C, D
Duration of travel, days			
≤30	4134 (59)	8994	A, C, D
>31 ^b	2597 (37)	8572	—
Interval time from travel to presentation, weeks			
≤1	2789 (40)	4750	A, B, C, D
1-6	2437 (35)	5762	A, B, C, D
>6 ^b	1511 (22)	7012	—
Recorded pretravel encounter			
No ^b	2535 (36)	5857	—
Yes	3488 (50)	9577	A, D
Unknown	840 (12)	2309	A, D
Total	6957 (28)	17,963	—

NOTE. A, variable was significant in sub-Saharan Africa regression; B, variable was significant in Southeast Asia regression; C, variable was significant in Latin American regression; D, variable was significant in south-central Asia regression; NS, variable was not significant in any multiple logistic regression.

^a Two-sided *P* < .05 determined using the Wald test is considered to be statistically significant.

^b Reference group in multivariate logistic regressions.

Table 3. Regional distribution of ill travelers with fever and major diagnosis groups, by region of likely exposure, for ill returned patients with fever (6957 patients with fever among 24,920 ill returned travelers).

Region of travel	No. of travelers who had fever	Fever ^a	Percentage of travelers, by condition						
			Systemic febrile illness	Malaria	Dengue	Undiagnosed febrile illness	Respiratory illness	Gastrointestinal illness	Vaccine-preventable illness
Oceania/Pacific Islands	156 ^b	51	68	59	5	12	10	4	1.9
Sub-Saharan Africa	2568	41	49	42	1	19	10	10	1.0
Southeast Asia	1219	33	34	7	18	22	17	17	2.1
South-central Asia	882	27	32	7	9	20	14	22	9.9
Northern Asia	133	24	8	1	0	26	39	11	7.5
Eastern Europe	65	33	14	1	0	14	29	25	10.9
Northern Africa	328	21	2	0	1	13	13	38	4.4
Caribbean and Central and South America	1044	18	25	0	9	26	13	15	2.2
Western Asia	89	18	12	1	0	31	16	18	2.2
United States, Canada, Western Europe, Australia, and New Zealand	177	15	14	0	0	28	25	9	5.1
Missing travel data	45	24	0	13	0	28	12	16	4.4
Multiple travel exposures	356	19	12	4	1	26	17	15	3.9
Total	6957	28	25	21	6	22	14	15	3.4

^a Percentage of travelers to the area who had fever.

^b Destination: Papua New Guinea, 51%; Vanuatu, 11%; and Solomon Islands, 10%. Origin of travelers: Australia, 40%; United States, 10%; Germany, 12%; New Zealand, 7%; and Israel, 7%.

From Wilson, M., et al. Fever in Returned Travelers: Results from the GeoSentinel Surveillance Network. Clin Infect Dis 2007; 44: 1560-8

Proportional morbidity (number per 1000 ill returned travelers)

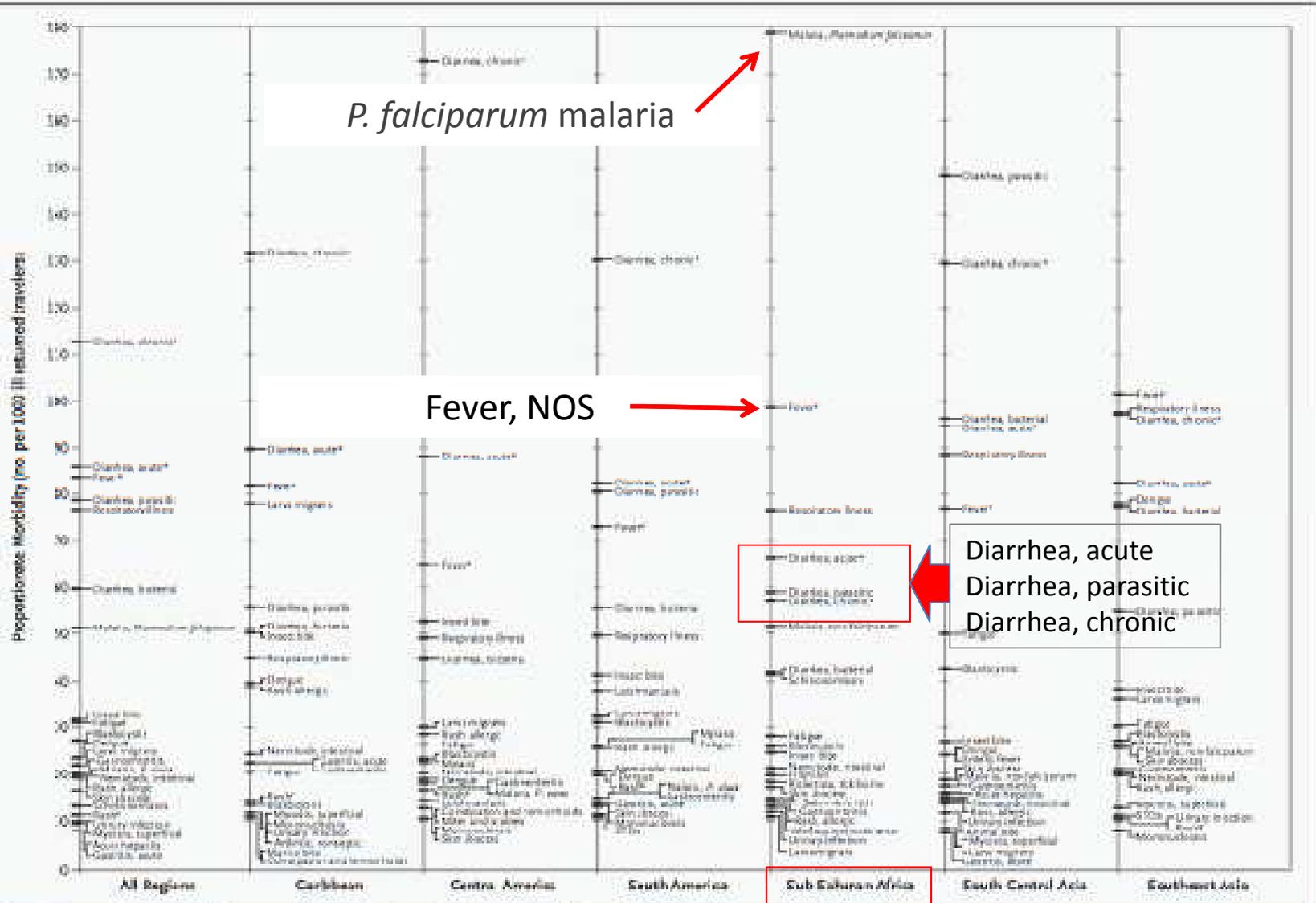


Figure 2. Proportionate Morbidity among Ill Travelers Returning from the Developing World, According to Region of Travel. The proportions are shown, not incidence rates, of each of the top 22 specific diagnoses for all ill returned travelers within each of the regions. STD denotes sexually transmitted disease. Asterisks indicate syndromic diagnoses for which specific etiologic diagnoses could not be assigned.

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Assumptions about your practice

- **Travel history:** you'll know this well since you are deploying with your unit
- **Vaccination history:** you'll know this well since your unit will generally be UTD
- ***Activity based risks:*** more of an unknown
 - Food intake/ingestions (crayfish, snails, slugs) ❖
 - Animal contact (rabies, tularemia, leptospirosis)
- **Vector exposure** and use of PPMs
- **Freshwater** exposure
- **Barefoot** exposure
- **Sexual** exposure



***Achitina fulica*,**
the giant African land snail

***Vaginulus plebeius*,**
the intermediate host of
Angiostrongylus costaricensis



ORIGINAL ARTICLE



The NEW ENGLAND
JOURNAL of MEDICINE

An Outbreak of Eosinophilic Meningitis Caused by *Angiostrongylus cantonensis* in Travelers Returning from the Caribbean

Trevor J. Slom, M.D., Margaret M. Cortese, M.D., Susan I. Gerber, M.D., Roderick C. Jones, M.P.H., Timothy H. Holtz, M.D., M.P.H., Adriana S. Lopez, M.H.S., Carlos H. Zambrano, M.D., Robert L. Sufit, M.D., Yuwaporn Sakolvaree, M.Sc., Wanpen Chaicumpa, Ph.D., Barbara L. Herwaldt, M.D., M.P.H., and Stuart Johnson, M.D., D.T.M.&H.

N Engl J Med 2002; 346 (9): 668-75, Feb 28

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Dangerous Lung Worms Found in People Who Eat Raw Crayfish

ScienceDaily (May 26, 2010) — If you're headed to a freshwater stream this summer and a friend dares you to eat a raw crayfish -- don't do it. You could end up in the hospital with a severe parasitic infection.

See Also:

Health & Medicine

- Today's Healthcare
- Diseases and Conditions
- Infectious Diseases

Plants & Animals

- Pests and Parasites
- Bacteria
- Microbiology

Reference

- Salmonella infection
- Tularemia
- Upper respiratory tract infection
- Candidiasis

Physicians at Washington University School of Medicine in St. Louis have diagnosed a rare parasitic infection in six people who had consumed raw crayfish from streams and rivers in Missouri. The cases occurred over the past three years, but three have been diagnosed since last September; the latest in April. Before these six, only seven such cases had ever been reported in North America, where the parasite, *Paragonimus kellicotti*, is common in crayfish.

"The infection, called paragonimiasis, is very rare, so it's extremely unusual to see this many cases in one medical center in a relatively short period of time," says Washington University infectious diseases specialist Gary Weil, MD, professor

of medicine and of molecular microbiology, who treated some of the patients. "We are almost certain there are other people out there with the infection who haven't been diagnosed. That's why we want to get the word out."

Paragonimiasis causes fever, cough, chest pain, shortness of breath and extreme fatigue. The infection is generally not fatal, and it is easily treated if properly diagnosed. But the illness is so unusual that most doctors are not aware of it. Most of the patients had received multiple treatments for pneumonia and



Eating raw crayfish can result in a severe parasitic infection. (Credit: Robert Boston)

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Breaking News

... from NewsDaily.com

THE AMERICAN LUNG FLUKE, *PARAGONIMUS KELLICOTTI*, IN A CAT MODEL

Peter J. Weina,* and Douglas M. England†

Departments of Zoology and Pathology, University of Wisconsin, Madison, Wisconsin 53706

ABSTRACT: Twenty-four specific-pathogen-free domestic cats were infected orally with from 2 to 30 *Paragonimus kellycotti* metacercariae and followed for 2–61 wk. Following infection by metacercarial cysts dissected from crayfish, the lungs of the cats undergo changes of intense eosinophilic pneumonia, granulomatous pneumonitis, squamous epithelial-lined cyst formation of bronchogenic origin, and finally (late in infection) partial resolution of the host response. Bronchograms and mechanical probing illustrate the patency of cyst communication with bronchi. The modulation of the host response and adaptive changes in the host lung tissue are seen late in infection and have previously been unreported or underemphasized. These adaptive responses may account for the number of asymptomatic cases accidentally found in veterinary patients and the difficulty in prompt and proper diagnosis in human cases.

Human infection by the lung trematode *Paragonimus westermani* is well recognized. However other species of *Paragonimus* widely distributed over 3 continents have been reported as causing paragonimiasis in humans (Bunnag and Harinasuta, 1984).

American paragonimiasis results from the ingestion of raw or undercooked crayfish containing the metacercarial cysts of *Paragonimus kellycotti*. Infections are distributed widely in wild and domestic carnivores (Nielsen, 1955; Bisgard and Lewis, 1964; Herman and Helland, 1966; Rendano, 1974; Presidente and Ramsden, 1975; Dubey et al., 1978). Recent reports of human infection with this species (Pachuncki et al., 1984; Mariano et al., 1986) may suggest that the parasite is more prevalent than recognized.

An animal model to understand better the host-parasite interaction would be of value. Cats are excellent hosts for *P. kellycotti* and display pulmonary changes similar to those described in humans infected with *P. westermani* (Beland et al., 1969; Hoover and Dubey, 1978; Minh et al., 1981; Spencer, 1985). In this study, 24 domestic cats were given various numbers of metacercarial cysts from naturally infected crayfish, and the

MATERIALS AND METHODS

Twenty-four specific-pathogen-free domestic cats were obtained from the Research Animal Resource Center at the University of Wisconsin—Madison and maintained in a colonial setting in the Department of Zoology animal quarters.

Paragonimus kellycotti metacercariae were dissected from naturally infected crayfish obtained by dip net in Honey Creek, Sauk County, Wisconsin. The metacercariae were fed to cats in doses ranging from 2 to 30 by placing the cysts on the back of the tongue and rinsing the throat with water.

Cats were observed for clinical symptoms (respiratory difficulties, lethargy, etc.) throughout the infections.

Cats were killed from 2 to 61 wk after infection by injection with ketamine and xylazine in concert prior to exsanguination. Two postmortem x-rays (Picker, GX-850) and bronchograms were taken to outline the bronchial tree and to demonstrate relative position of parasite cysts within the bronchi.

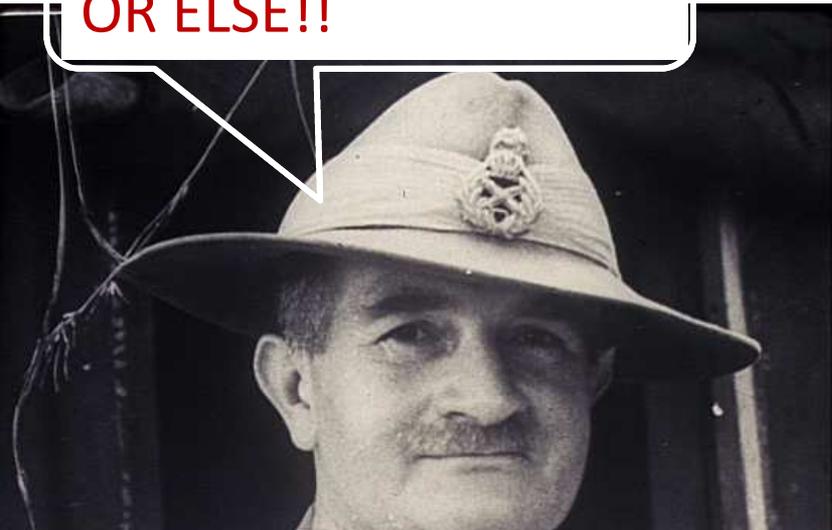
A complete necropsy was performed on all animals. Lungs were perfused and inflated with a 10% neutral buffered formalin solution introduced under pressure from a large syringe in the trachea. Subsequently, the trachea was clamped and the lungs floated in a formalin bath for a minimum fixation time of 2 days. Continuity of the cyst with a bronchus or bronchiole was demonstrated by passing a metal probe from airways into cysts containing the parasites. Lungs were then cut sagittally into 0.5–1.0-cm slices. One- to two-centimeter



Assumptions about your practice

- Travel history: you'll know this well since you are deploying with your unit
- Vaccination history: you'll know this well since your unit will generally be UTD
- Activity based risks: more of an unknown
 - Food intake/ingestions (crayfish, snails, slugs)
 - Animal contact (rabies, tularemia, leptospirosis)
- **Vector exposure and use of PPMs**
- **Freshwater exposure**
- **Barefoot exposure**
- **Sexual exposure**
- **Adherence to antimalarial chemoprophylaxis**

Take your malaria pills
OR ELSE!!

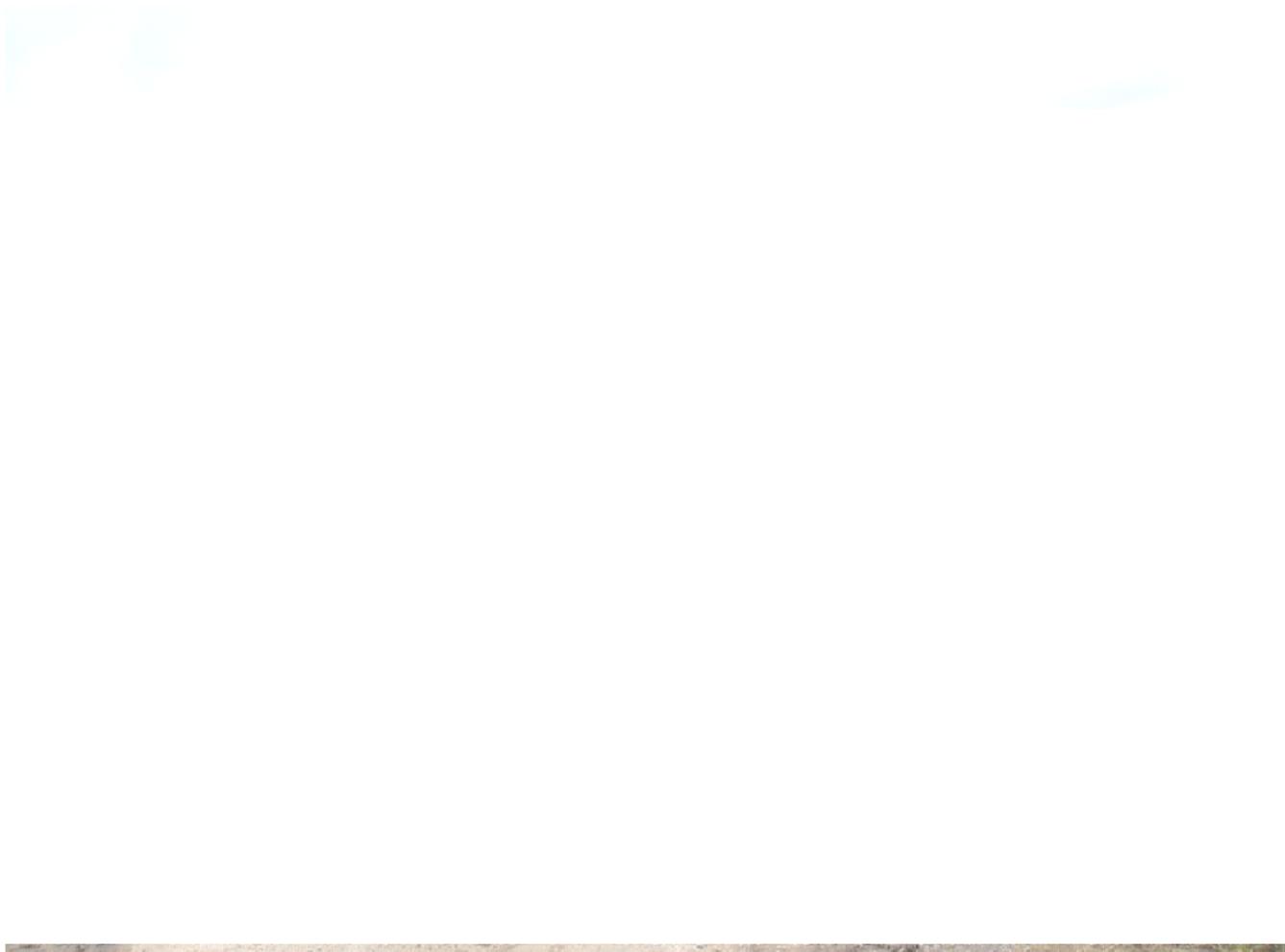


**"MORE THAN HALF THE
BATTLE AGAINST DISEASE IS
FOUGHT NOT BY DOCTORS,
BUT BY REGIMENTAL
OFFICERS"**

**GENERAL WILLIAM SLIM
Burma Theatre, WW2**

QUININE PARADE IN GREECE

Slide courtesy of Dr. Steven Craig
FROM: MACPHERSON, *MEDICAL SERVICES*
HYGIENE, V2, 1924



**Warehouse that Housed Marines at Roberts International Airport, Liberia, during
August 2003 peacekeeping deployment**

An Outbreak of *Plasmodium falciparum* Malaria in U.S. Marines Deployed to Liberia

Timothy J. Whitman,* Philip E. Coyne, Alan J. Magill, David L. Blazes, Michael D. Green, Wilbur K. Milhous, Timothy H. Burgess, Daniel Freilich, Sybil A. Tasker, Ramzy G. Azar, Timothy P. Endy, Christopher D. Clagett, Gregory A. Deye, G. Dennis Shanks, and Gregory J. Martin*

Infectious Diseases Department, National Naval Medical Center, Bethesda, Maryland; Walter Reed Army Institute of Research, Silver Spring, Maryland; Infectious Diseases Clinical Research Program, Uniformed Services University, Bethesda, Maryland; Division of Parasitic Diseases, Centers for Disease Control and Prevention, Atlanta, Georgia; College of Public Health, University of South Florida, Tampa, Florida; Naval Medical Research Center, Silver Spring, Maryland; Infectious Diseases Division, Department of Medicine, State University of New York, Upstate Medical University, Syracuse, New York; U.S. Navy Environmental and Preventive Medicine Unit Seven, Naples, Italy; Australian Army Malaria Institute, Gallipoli Barracks, Australia

Abstract. In 2003, 44 U.S. Marines were evacuated from Liberia with either confirmed or presumed *Plasmodium falciparum* malaria. An outbreak investigation showed that only 19 (45%) used insect repellent, 5 (12%) used permethrin-treated clothing, and none used bed netting. Adherence with weekly mefloquine (MQ) was reported by 23 (55%). However, only 4 (10%) had serum MQ levels high enough to correlate with protection (> 794 ng/mL), and 9 (22%) had evidence of steady-state kinetics (MQ carboxy metabolite/MQ > 3.79). Tablets collected from Marines met USP identity and dissolution specifications for MQ. Testing failed to identify *P. falciparum* isolates with MQ resistance. This outbreak resulted from under use of personal protective measures and inadequate adherence with chemoprophylaxis. It is essential that all international travelers make malaria prevention measures a priority, especially when embarking to regions of the world with high transmission intensity such as west Africa.

“Good doctors are of no use without good discipline. More than half the battle against disease is not fought by doctors, but by regimental officers. It is they who see that the daily dose of mepacrine (anti-malarial chemoprophylactic drug used in WW II) is taken...if mepacrine was not taken, I sacked the commander. I only had to sack three; by then the rest had got my meaning.”

—Lieutenant General William Slim (1891–1970),
Burma Campaign, 1943

INTRODUCTION

than half were evacuated to U.S. military hospitals in Germany and Bethesda, Maryland. This report summarizes the clinical, laboratory, and epidemiologic features of an outbreak of malaria that was unique in severity of illness and attack rate after a brief exposure to a locale with high transmission intensity. It also discusses host and parasite factors that contributed to these apparent chemoprophylaxis failures.⁷

MATERIALS AND METHODS

In August 2003, 225 Marines with the 26th Marine Expeditionary Unit aboard U.S. Navy ships were deployed to Roberts International Airport outside the coastal city of Monrovia. Liberia has a tropical climate that includes fre-

“It has been said that a good history – listening to the patient – allows a diagnosis 90% of the time. *Nowhere is a complete and accurate history more important than when approaching a febrile traveler.*”

➤ Schwartz MD. Fever in the returning traveler, part one: a methodological approach to initial evaluation. *Wilderness and Environmental Medicine* 14; 24-32, 2003.

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Malaria, Other (cobalt)
Typhoid (red)
Dengue (teal)
Vivax malaria (green)
Falciparum malaria (yellow)

Incubation period as a guide to diagnosis of fever etiology

From Wilson, M., et al. Fever in Returned Travelers:
Results from the GeoSentinel Surveillance Network.
Clin Infect Dis 2007; 44: 1560-8

Common infections in travelers, by incubation period

Disease	Usual incubation period (range)	Distribution
<i>Incubation < 14 days</i>		
Malaria, falciparum	6-30 days (weeks to years)	Tropics, subtropics
Dengue	4-8 days (3-14 days)	Tropics, subtropics
Spotted fever rickettsiae	Few days to 2-3 weeks	Causitive species varies by region
Leptospirosis	7-12 days (2-26 days)	Widespread, more common in tropics
Enteric fever	7-18 days (3-60 days)	Indian subcontinent, South America
Malaria, vivax	8-30 days (often > one month)	Tropics, subtropics
Influenza	1-3 days	Worldwide, including during transit
Acute HIV	10-28 days (10 days – 6 weeks)	Worldwide
Legionellosis	5-6 days (2-10 days)	Worldwide
Encephalitis, arboviral (e.g. JE, TBE, WNV, etc)	3-14 days (1-20 days)	Specific agents vary by region

Wilson ME. Fever in returned travelers. *CDC Health Information for International Travel, 2010*. Table 4-5, page 286

Disease	Usual incubation period (range)	Distribution
<i>Incubation > 14 days to 6 weeks</i>		
Malaria, enteric fever, leptospirosis	See previous table	See previous table
Hepatitis A	28-30 days (15-50 days)	Most common in developing countries
Hepatitis E	26-42 days (2-9 weeks)	Widespread
Acute Schistosomiasis (Katayama syndrome)	4-8 weeks	Sub Saharan Africa most commonly
Amoebic liver abscess	Weeks to months	Most common in developing countries

Wilson ME. Fever in returned travelers. *CDC Health Information for International Travel, 2010* . Table 4-5, page 286

An Analysis of Fevers of Unknown Origin in American Soldiers in Vietnam

JOHN J. DELLER, JR., LT. COL., MC, USA, and PHILIP K. RUSSELL, MAJ., MC, USA
 Long Binh, South Vietnam

A NUMBER OF FEBRILE DISEASES endemic in Vietnam are characterized by the sudden onset of high fever, chills, and headache. Although the classical varieties of the arbovirus diseases, scrub typhus and malaria, as well as a number of other tropical febrile illnesses, have been well described (1-7), the differential diagnosis of these tropical diseases remains a real challenge.

In an attempt to define these "fevers of unknown origin," 110 patients presenting in this fashion in whom a more precise diagnosis could not be made within 24 hr of admission to the 93rd Evacuation Hospital, Long Binh, South Vietnam, were studied. Serologic, virologic, and bacteriologic methods were used to confirm the diagnosis in all cases.

MATERIALS AND METHODS

All patients admitted to the medical service from April 1, 1966, to August 1, 1966, with fever (over 101 F), chills (frank chills or chilliness), headache (of any degree), a negative malaria smear, and in whom a specific diagnosis could not be made were admitted to the study.

Patients were evaluated according to a standard clinical protocol that recorded epidemiologic data, a narrative history, and specific symptom, physical examination, and laboratory checklists that were monitored daily for the first 7 days of hospitalization.

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From the 93rd Evacuation Hospital, Long Binh, South Vietnam.

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Clinical feature	Dengue	Chikungunya	Scrub Typhus	Malaria
Epidemiology				
Camp, urban	+++	+++	--	--
Jungle	--	--	+++	+++
Fever, degrees F				
< 104	+++	+++	+	--
> 104	--	--	++	+++
Arthralgias				
Tender adenopathy	++ (early)	+++	+++ (later)	--
Tender liver/spleen				
Rash	+	++	++	--
Petechiae/tourniquet test positive				
WBC, /mm ³				
< 5,000	++	++	--	--
> 5,000	+	+	+++	+++
SGOT > 50 units				
	--	--	--	+++

Deller JJ and Russell PK.
Ann Intern Med 66:
 1129-43, 1967

Outline

- Introduction
- Epidemiology of illness in the returned traveler
- General assumptions
- Clinical scenarios
- **Specific pathogens of interest**
- Sources of information
- Final comments

Common clinical findings and associated infections

Fever + **rash** → rickettsioses, typhus, Dengue, mening/GC, acute HIV

Fever + **chancre** (or 'tache noir') → ATBF, Trypanosomiasis

Fever + **abdominal pain** → Typhoid, amoebic dysentery/abscess

Fever + **myalgias/artralgias** → Dengue, Chikungunya

Fever + **hemorrhage** → VHF (YF, Dengue), mening, leptospirosis

Fever + **jaundice** → YF, leptospirosis

Fever + **eos** → Katayama syndrome, Trichinellosis, other worms

Fever + **meningeal signs** → usual suspects, Angiostrongylus

Fever NOS + **normal or low WBC** → malaria, visceral leish, Dengue, rickettsiae, Chikungunya

Fever + **tender lymphadenopathy** → *Yersinia pestis*

Fever **persisting > 2 weeks** → see table

Fever with **delayed onset (> 6 weeks after return)** → *P. malariae*, *P. vivax*, TB, visceral leish,

Initial studies for diagnosis in returned travelers with unexplained fever

- Thick and thin smears for malaria (supplement with rapid diagnostic tests, as available)
 - Complete blood count with differential and platelet estimate
 - Liver function
 - Blood cultures
 - Urinalysis
 - Chest X-rays
- * Additional tests will depend on specific findings and exposures

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Key websites

- www.cdc.gov/travel/page/yellowbook-2012-home.htm The Yellow Book
- www.cdc.gov/dpdx Parasitic Diseases diagnosis
- www.istm.org/geosentinel/main.html
- www.promedmail.org Searchable outbreak info
- AFMIC/NCMI
- www.tropnet.net European Network on Imported Infectious Disease Surveillance

Additional websites

- www.fallingrain.com elevation and rainfall data
- www.healthmap.org outbreak information
- www.lib.utexas.edu/maps *outstanding* map collection!
- <http://www.cdc.gov/vaccines/pubs/pinkbook/default.htm> the 'Pink Book' on vaccines

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Take home point number one:

alaria

**ALWAYS include malaria in the differential of fever
in a returnee from Africa**

Keep in Mind that...

- Initial symptoms of life-threatening and self-limited infections can be ***identical***.
- **Malaria** is the most common cause of acute undifferentiated fever after travel to sub-Saharan Africa and to some other tropical areas.
- Patients with **malaria** may be afebrile at the time of evaluation but typically give a history of chills.
- **Malaria, especially *falciparum*, can progress rapidly.**
Diagnostic studies should be done promptly and **treatment instituted *immediately*** if malaria is diagnosed.
- A history of taking malaria chemoprophylaxis **does not exclude the possibility of malaria.**
- Patients with **malaria** can have prominent **respiratory** (including adult respiratory distress syndrome), GI, or central nervous system findings.

Also Keep in Mind that...

- Viral hemorrhagic fevers are important to identify but are **rare** in travelers; bacterial infections, such as

- **leptospirosis**
- **meningococemia** and
- **rickettsial** infections

can also cause fever and hemorrhage and should be always be considered because of the need to institute prompt, specific treatment.

- **Sexually transmitted infections**, including acute HIV, can cause acute febrile infections.
- Consider infection control, public health implications and requirements for reportable diseases.
- Fever in returned travelers is often caused by **common, cosmopolitan infections**, such as pneumonia and pyelonephritis.
Common things occur commonly.

**Take home point
number two:**

Doxycycline??

**Consider empiric
doxycycline**

References

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Any questions??

