

LETHAL INFECTIONS ASSOCIATED WITH TRAVEL

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The Extent of the Problem

- ▣ Each year, an estimated 50 million travelers from Western countries visit tropical regions of the world, these numbers are rapidly growing

World Tourism Organization, 2010

http://www.unwto.org/facts/eng/pdf/highlights/UNWTO_Highlights10_en_LR.pdf

Global Spread of Disease

- ▣ Since 1970 ≥ 1 new diseases have emerged /yr
- ▣ Now ~ 40 diseases unknown a generation ago
- ▣ In last 5 years WHO has verified >1100 epidemics worldwide
- ▣ Cholera, yellow fever, meningococcal diseases, SARS H5N1, H7N9, Ebola, Marburg & Nipah virus, West Nile, Dengue, MERSCoV



FLIGHT **zh**
BY SHANTAR **aw**
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Diagnosis: History

- ▣ Age, sex, residence, comorbid illness, medication
- ▣ Symptoms, date of travel, countries visited
- ▣ HCW & lab workers often particularly at risk
- ▣ Occupational/non-occupational contacts; bats, animals, hunters, bush meat
- ▣ Contact with known/suspected cases or known outbreaks
- ▣ Mosquitos, ticks, rural dwelling

Implicated Tropical Diseases

Viral infections or syndromes

Avian influenza
DHF/DSS
Lassa fever and other tropical hemorrhagic
fevers
Japanese encephalitis and other tropical
encephalitides
Rift Valley fever
Yellow fever

Bacterial infections

Anthrax
Carrion's disease*
Epidemic typhus
Leptospirosis
Melioidosis
Murine typhus
Paratyphoid fever
Plague
Relapsing fever
Scrub typhus
Spotted fever group rickettsioses†
Typhoid fever

Protozoan infections

East African sleeping sickness‡
Falciparum malaria
Knowlesi malaria

GeoSentinel Study 1996–2011: Tropical/Subtropical Diseases

- ▣ 82 825 ill western travelers to subtropical /tropical regions that sought medical care
- ▣ 3 655 (4.4%) with 3 666 diagnoses had an acute, potentially life-threatening disease
- ▣ Falciparum malaria (76.9%), typhoid (11.7%), paratyphoid (6.4%) & leptospirosis (2.4%)
- ▣ 91% had fever, 60% hospitalized, 0.4% died
- ▣ 62% reported from Europe, 20% from North America, 4% NZ/Australia, 14% elsewhere

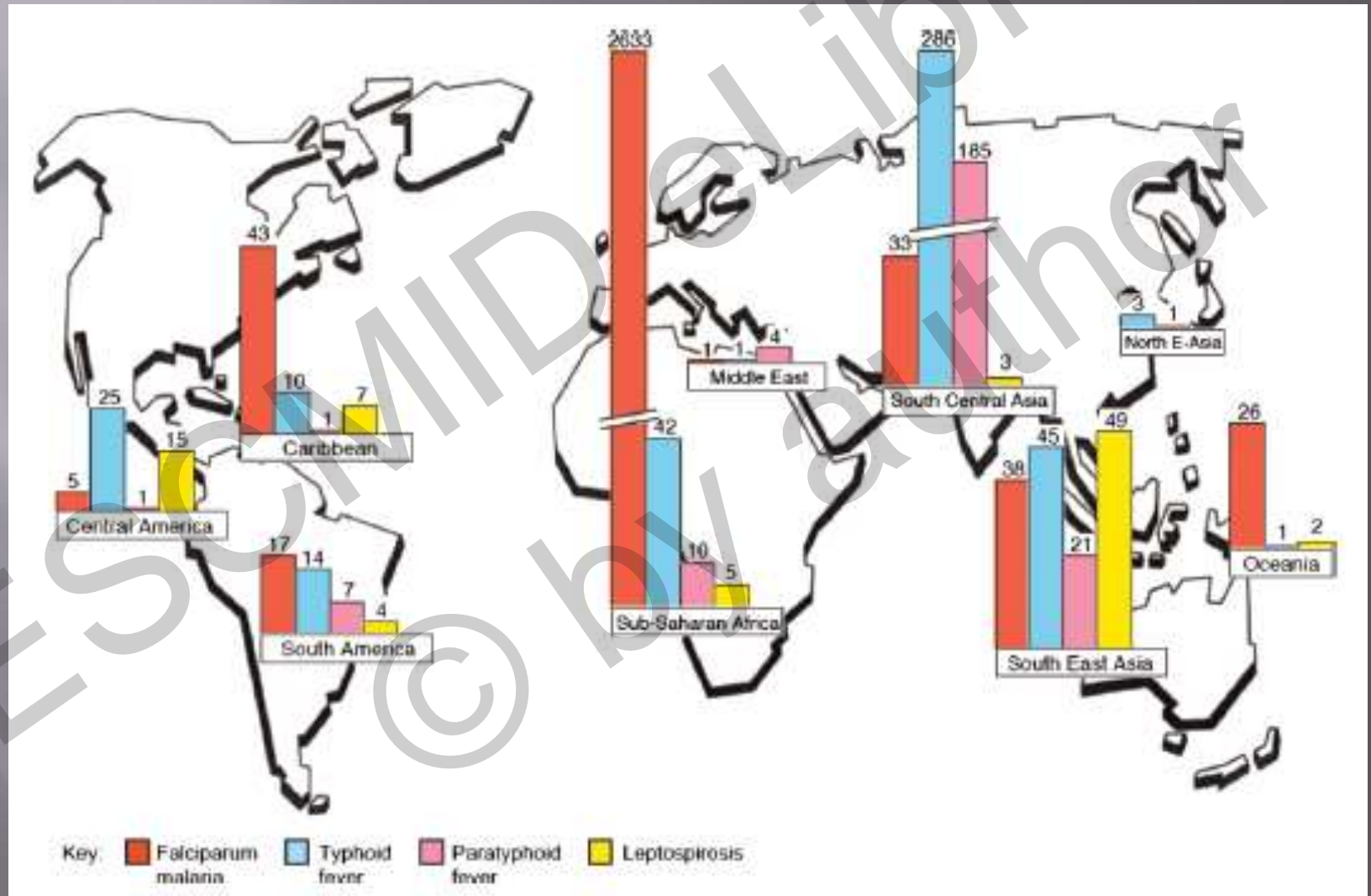
GeoSentinel Study 1996–2011: Tropical/Subtropical Diseases

- ▣ No cases of anthrax, plague, Bartonella (bacilliformis infection), epidemic typhus, diphtheria, avian influenza, Lassa or other African VHFs, yellow fever, Rift Valley fever, or tropical encephalitides
- ▣ Dengue HF/shock syndrome diagnosed in 18 constituting 0.9% of all dengue cases (N = 1 910); 30% of DHF/DSS were contracted in Thailand

GeoSentinel Study 1996–2011: Tropical/Subtropical Diseases

- ▣ 210 cases of paratyphoid, 79% from South Central Asia; India 38%, Nepal 30%; Pakistan 10%; Bangladesh 11.5%
- ▣ Leptospirosis diagnosed in 88; most from SEA; Thailand 22%, Laos, 13%, Indonesia 6.7%
- ▣ Rickettsioses in 58
- ▣ Relapsing fever in 7; 5 from sub-Saharan Africa
- ▣ Melioidosis diagnosed in 6

Lethal Tropical Diseases



Community Acquired Pneumonia

- ▣ Any patient can acquire CAP
- ▣ Generally there are guidelines for management of the common causes such as *S. pneumoniae*, *M pneumoniae*, *C pneumoniae*, viruses etc
- ▣ However certain infections in travellers that require different forms of therapy may not initially be considered.

Community Acquired Pneumonia: *S aureus*

- ▣ Usually fulminant with rapid onset respiratory failure & MODS ± shock & death
- ▣ Frequently pulmonary necrosis, abscess, empyema especially with Panton Valentin Leukocidin (PVL)- cytotoxin responsible for leukocyte destruction & tissue necrosis
- ▣ Leucopenia (2500/cu.mm) characteristic & may be an inverse biomarker of PVL burden.
- ▣ Risk factors: colonization or infection with *S. aureus* & preceding influenza like illness

Francis Clin Infect Dis 2005

Rello International Journal of Infectious Diseases 2016

Community Acquired pneumonia: Legionnaires disease

- ▣ Pneumonia is the most common presentation: may be severe with MODS & death
- ▣ Characteristic clinical findings: relative bradycardia, hyponatraemia, elevated CPK, diarrhea, confusion & impaired liver & kidney-function
- ▣ Diagnosis: urine antigen for group 1 *L. pneumophila* (80% of cases), PCR

CAP: Melioidosis (*Burkholderia pseudomallei*)

- ❑ Endemic GNB: SE Asia, north Australia, India, south China, Taiwan
- ❑ Inoculation from contaminated soil/water through abrasions or inhalation with haematogenous spread
- ❑ Horizontal transmission rare
- ❑ Most common cause of fatal CA bacteraemia & pneumonia in NE Thailand & Darwin
- ❑ Variable severity & presentation: 50% CAP (nodular infiltrates or consolidation \pm shock), abscesses, osteomyelitis, arthritis
- ❑ Risks: diabetes/immunosuppression, chronic lung disease

Community Acquired Pneumonia: Influenza

- ▣ 2009 influenza A(H1N1)pdm09 pandemic >18,500 deaths reported & global estimates 15 X higher.
- ▣ 1° risk factors: young/middle aged (>60% <65yrs), pregnancy, morbid obesity immunocompromise
- ▣ Influenza increases risk of *S. pneumoniae* & *S.aureus*
- ▣ Those with severe disease deteriorate acutely after 4-5 days- severe ARDS, shock & often MODS
- ▣ Pathology: intense inflammatory/ hemorrhagic CAP

Napolitano JAMA 2014

Rello International Journal of Infectious Diseases 2016

Avian Influenzas: H5N1 & H7N9

- ▣ Avian influenzas remain a potential threat
- ▣ Travelers with unexplained ARDS with contact with birds in affected areas should be screened
- ▣ H5N1 reported from 17 countries - currently most prevalent in Egypt
- ▣ H5N1: Overall (Dec 2016) 856 cases (452 deaths)
- ▣ H7N1: Between March 2013- Feb 6, 2017; 1101 cases, mortality 35%: China has reported 301 cases, 65 deaths since Dec 1 2016

http://www.who.int/influenza/human_animal_interface/2016_12_19_tableH5N1.pdf?ua=1

http://www.wpro.who.int/outbreaks_emergencies/H7N9/en

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Middle East Respiratory syndrome Coronavirus (MERS-CoV)

- ▣ 10yrs post SARS (with 8000 cases & 775 deaths), MERS-CoV appeared in Saudi
- ▣ Currently (Dec 2016) 1879 cases, 659 deaths, 27 countries
- ▣ MERS-CoV differs from SARS -binds different receptors & camels are the primary reservoir host although the means of transmission from these animals is poorly understood

Middle East Respiratory syndrome Coronavirus (MERS-CoV)

- ▣ Transmission occurs between humans, epidemic potential less than SARS
- ▣ Not always severe, ranges from ILI to severe CAP
- ▣ Most severe patients have co-morbidities; diabetes, CRF, immunocompromise, chronic lung disease
- ▣ Supportive care is central; Ribavirin & interferon combinations have modest effects in rhesus macaques
- ▣ Convalescent plasma had best evidence to reduce duration & mortality when used early in SARS
- ▣ Diagnosis: RT PCR

Malaria

- ▣ Transmitted in 108 countries; in 2010 an estimated 216 million cases & 655 000 deaths (almost all falciparum)
- ▣ > 85% of cases & 90% of deaths occur in sub-Saharan Africa, mainly children <5 & pregnant women
- ▣ Severe disease due to extensive sequestration of parasitised erythrocytes with microvascular obstruction proportional to *clinical* severity, plasma lactate & base deficit
- ▣ Significant organ dysfunction occurs; hypoglycaemia, ARDS, AKI, coma

White Lancet 2014;

White N Engl J Med 2014

Malaria

- ▣ Mortality in travellers caused mainly by late recognition & delayed therapy
- ▣ ALWAYS take a travel history
- ▣ If any doubt perform slide microscopy & rapid antigen tests if necessary
- ▣ Treatment of choice -parenteral artemisinins although resistance is emerging.

VHF

- ▣ Caused by infection with zoonotic RNA viruses.
- ▣ Aetiology differs, clinical presentation often similar: abrupt onset of fever, headache, myalgia, lumbar pain, nausea, vomiting, diarrhoea, petechial or maculopapular rash
- ▣ Leucopenia, thrombocytopenia, elevated AST/ALT, progressively abnormal INR, PTT & haemorrhage (not a constant feature) may supervene about day 5
- ▣ In EBV outbreak a minority had overt haemorrhage
- ▣ Diagnosis: RT PCR

Family	Diseases	Transmission
Arenaviridae	South American HF (Junin) Lassa fever	Rodent urine Rodent urine
Bunyaviridae	Rift valley fever CCHF Hantavirus (HV) HV with renal syndrome	Mosquito/ ticks Ticks Rodent Rodent
Filoviridae	Filovirus HF Ebola, Marburg	Bats
Flaviviridae	Yellow fever Dengue HF Kyasanur forest disease Omsk HF	Mosquito Mosquito Tick Tick/rodent

VHF

- ▣ Travel associated VHFs relatively frequent in RSA
- ▣ African HF viruses: Arenaviridae (Lassa & Lujo), Bunyaviridae (CCHF & Rift Valley), Filoviridae (EBV & Marburg)
- ▣ Lassa frequent in Sierra Leone, Guinea, Liberia & Nigeria; ± 500 000 cases annually
- ▣ Spread via aerosolised urine & faecal matter
- ▣ In 2008: VHF outbreak in Jhb of newly identified Lujo virus (Lusaka-Johannesburg): 5 cases, one survivor

Gear [BMJ1975](#)

Richards S [Afr Med J 2015; DOI:10.7196/SAMJnew.8330](#)

Richards S [Afr Med J 2015; DOI:10.7196/SAMJnew.8168](#)

Sewlall NH, Richards GA et al [PLoS Negl Trop Dis 2014](#)

VHF: Isolation Precautions

- ▣ Train designated HCW in isolation & management
- ▣ Train all HCW to identify possible EVD & refer
- ▣ Monitor:
 - isolation & safety practice by ID staff 24/7
 - Monitor HCW in contact with daily temperature
- ▣ Inform all relevant staff of suspected/proven EVD
- ▣ Inform Communicable Disease Control officials of national and provincial DOH

Dengue

- ▣ Acute, mosquito borne febrile syndrome usually follows a benign course
- ▣ 3.9 billion people in 128 countries are at risk
- ▣ Pre 1970, 9 countries had dengue epidemics
- ▣ Now endemic in >100 countries
- ▣ 2nd most common cause of fever in travellers returning from low/middle-income countries
- ▣ 2015: Philippines reported >169 000 cases, Malaysia >111 000 a 59.5% & 16% increase vs 2014. Brazil reported >1.5 million cases 3 x >2014

Brady PLoS Negl Trop Dis. 2012

<http://www.who.int/mediacentre/factsheets/fs117/en/>

Dengue

- ▣ Aedes mosquitoes: Incubation: 4–7 days
- ▣ High fever (40°C/104°F) plus 2 of: severe headache, retro-orbital pain, muscle & joint pain, nausea, vomiting, swollen glands or rash
- ▣ Severe dengue potentially deadly due to capillary leak, ARDS, haemorrhage, shock, MODS
- ▣ Rapid diagnostic tests: NS1 antigen & IgM ELISAs, RT-PCR
- ▣ Treatment supportive

Yellow Fever

- ▣ Incubation 3–8 days, transmitted by *Aedes*, *haemagogus* & *sabethes* mosquitoes
- ▣ South America, Africa
- ▣ Most are mild & self-limited: fever, headache, myalgia, malaise
- ▣ Presentation divided into 3 stages: infection, remission & intoxication
- ▣ 15% are more ill with neutropenia & elevated AST & ALT 48-72 hours after initial symptoms

Yellow Fever

- ▣ Recent reemergence in rural Brazil; concern about epidemic potential if not contained before reaching urban areas.
- ▣ Since Feb 2017 234 confirmed infections, 80 deaths
- ▣ Large urban outbreaks also occurred in Angola & spread to DRC in December 2015, with 961 cases & 137 deaths

Yellow Fever

- ▣ In 15-25% humoral immunity reduces viraemia & is responsible for return of symptoms
- ▣ Fever, vomiting, abdominal pain, AKI, haemorrhage, petechiae, ecchymoses, epistaxis & bleeding from gums & venipuncture sites
- ▣ Jaundice & transaminitis worsens & DIC may develop (Hepatorenal syndrome has a mortality of 20-50%}; 7-10 days after symptoms onset
- ▣ Treatment supportive

Wallace <http://emedicine.medscape.com/article/232244-workup#c7>
Monath Yellow fever. J Clin Virol. 2015 Mar. 64:160-73.

Leptospirosis

- ▣ *Leptospira* species: acquired by contact with urine/reproductive fluids from infected animals or with contaminated water or soil through abrasions, conjunctiva & mucous membranes
- ▣ Mostly travellers from SEAsia: incubation 2d- 3wks
- ▣ Untreated, some serogroups (*L. icterohaemorrhagiae*) have substantial mortality
- ▣ Severe forms (Weil disease) occur in 5–10%; Jaundice, AKI, hemorrhage (especially pulmonary), cardiac arrhythmias, pneumonitis, hemodynamic collapse
- ▣ Penicillin, doxycycline, cephalosporins equal efficacy

African Trypanosomiasis: Sleeping Sickness

- ▣ *Trypanosoma brucei gambiense*: 24 countries (west/central Africa 97% of cases); chronic infection, months-years with no symptoms; then CNS involvement
- ▣ *Trypanosoma brucei rhodesiense*: <3% of cases- 13 countries in east/southern Africa- rapid onset acute infection months- weeks after infection- invades CNS
- ▣ Multiplies in subcutaneous tissues, blood & lymph: crosses the BBB; fever, headache, joint pain & rarely DIC- Without treatment, sleeping sickness is fatal
- ▣ Diagnosis: serology (*T.b.gambiense*) & microscopy

Conclusion

- ▣ With so many travellers worldwide & with deforestation increasing exposure to previously isolated areas, a high index of suspicion is necessary & a very good history critical to early diagnosis and isolation if necessary