Educational Workshop

EW11: "Final destination ICU" - cases of severely ill travellers

Arranged with ESGCIP & ESGITM

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Faculty:    Hakan Leblebicioglu, Samsun, TR
            Garyfallia Poulakou, Athens, GR
            Nicholas J. Beeching, Liverpool, UK
            Allison McGeer, Toronto, CA

Marked in red = no handouts available
Fever with hemorrhagic manifestations

Case with a tick bite

- A 70-year old British man
- Recent trip to Bulgaria
- He was bitten by a tick while outdoors
- He removed the tick that evening without difficulty
- Approximately five days previously, he had removed a tick from a cat and crushed it between his fingers

Clinical features

- Fever, sweats, cough, sore throat, myalgia, headache, diarrhea and two episodes of collapse
- A petechial rash on his legs and bilateral crepitations on chest auscultation
- Blood count and chemistry
  - Platelet count of 26 × 10^9/L (norm: 150–400 × 10^9 /L)
  - Neutrophils of 1.1 × 10^9/L (norm: 2.0–7.5 × 10^9/L)
  - ALT, at 64 units (U)/L (norm: 10–40 U/L)
What is your diagnosis?
- Malaria
- Dengue
- Rickettsial infection
- Ebola Virus Disease
- Crimean Congo Hemorrhagic Fever

Approach to the febrile traveller

5W1H
Leblebicioglu - Fever with haemorrhagic manifestations

**Travel history**

- Destination
- Prophylaxis
- Returning traveller
- Activities
- Immunization
- Exposures

**Physical examination**

- CNS status
- Temperature
- Bleeding
- Pain
- Murmur, cardiac rhythm
- Pulse, regular?
- Pulmonary
- Blood pressure
- Abdomen
- O2 Saturation
- Lymphadenopathy
- Respiratory rate
- Rash, other skin symptoms

**Incubation time – migrants infected in their country of origin**

- Chikungunya
- CCHF
- Dengue
- Tick typhus
- Salmonella typhi
- Malaria
- Leishmaniasis
- Tuberculosis
- HIV
- Echinococcosis
- Hepatitis B

<table>
<thead>
<tr>
<th>Disease</th>
<th>Incubation Period</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chikungunya</td>
<td>1 week</td>
</tr>
<tr>
<td>CCHF</td>
<td>1 month</td>
</tr>
<tr>
<td>Dengue</td>
<td>6 months</td>
</tr>
<tr>
<td>Tick typhus</td>
<td>1 year</td>
</tr>
<tr>
<td>Salmonella typhi</td>
<td>10 years</td>
</tr>
<tr>
<td>Malaria</td>
<td></td>
</tr>
<tr>
<td>Leishmaniasis</td>
<td></td>
</tr>
<tr>
<td>Tuberculosis</td>
<td></td>
</tr>
<tr>
<td>HIV</td>
<td></td>
</tr>
<tr>
<td>Echinococcosis</td>
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</tr>
<tr>
<td>Hepatitis B</td>
<td></td>
</tr>
</tbody>
</table>
Leblebicioglu - Fever with haemorrhagic manifestations

**Fever with hemorrhage**

- Viral hemorrhagic fevers  
  - Lassa, Ebola Marburg, Yellow fever, Crimean–Congo, Dengue, Hantaan  
- Rickettsial infections  
- Typhoid fever  
- Leptospirosis  
- Severe sepsis (DIC)  
- Infective endocarditis  
- Meningococcal septicemia

**Non infectious diseases**

- Vasculitis including Henoch–Schönlein purpura  
- Drug rashes  
- Idiopathic or thrombotic thrombocytopenic purpura  
- Hemolytic uremic syndrome  
- Acute leukemia  
- Collagen-vascular diseases
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Geographical distribution of EVD

Geographical distribution of CCHF

Geographic distribution of CCHF
Viral Hemorrhagic Fevers

- Lassa fever
  - West Africa
- Junin (Argentina HF)
  - South America
- Machupo (Bolivian HF)
  - South America
- Hantavirus
  - Diverse
- Yellow fever
  - Tropical Africa, Latin America
- Rift valley fever
  - Africa
- CCHF
  - Africa, Eurasia
- Omsk HF
  - Siberia
- Kyasanur Forest Disease
  - India
- Alkhurma HF
  - Saudi Arabia
- Severe fever with thrombocytopenia syndrome
  - Japan

VHF: Human to human transmission

- Ebola
- Marburg
- CCHF
- Lassa Fever
- Yellow fever
- Close contact with the blood secretions, organs or other body fluids of patients
- Needle stick injury
- Aerosol generating procedures

Hemorrhagic signs

- Archives of OMU Dept. of ID
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**Associated symptoms**

<table>
<thead>
<tr>
<th>Physical finding</th>
<th>Infection or disease implicated</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rash</td>
<td>Dengue, typhoid, rickettsial infections, syphilis, gonorrhoea, Ebola virus, brucellosis</td>
</tr>
<tr>
<td>Jaundice</td>
<td>Hepatitis, malaria, yellow fever, leptospirosis, relapsing fever</td>
</tr>
<tr>
<td>Lymphadenopathy</td>
<td>Rickettsial infections, brucellosis, dengue, HIV, Lassa fever, visceral leishmaniasis</td>
</tr>
<tr>
<td>Hepatomegaly</td>
<td>Amoebiasis, malaria, typhoid, hepatitis, leptospirosis</td>
</tr>
<tr>
<td>Splenomegaly</td>
<td>Malaria, relapsing fever, trypanosomiasis, typhoid, brucellosis, kala-azar, typhus, dengue</td>
</tr>
</tbody>
</table>

**Epidemiologic**

- Rickettsial infections, borela, Crimean-Congo haemorrhagic fever
- Dengue, meningococcal meningitis, Lassa fever, Marburg or Ebola viruses, Crimean-Congo haemorrhagic fever, Rift Valley fever, yellow fever, epidemic lassa haemorrhagic fever, Rocky Mountain spotted fever

**Clinical manifestations in West African Ebola Outbreak**

<table>
<thead>
<tr>
<th>Organ System</th>
<th>Clinical Manifestation</th>
</tr>
</thead>
<tbody>
<tr>
<td>General</td>
<td>Fever (87%), fatigue (76%), arthralgia (39%), myalgia (39%)</td>
</tr>
<tr>
<td>Neurological</td>
<td>Headache (53%), confusion (13%), eye pain (9%), coma (6%)</td>
</tr>
<tr>
<td>Cardiovascular</td>
<td>Chest pain (37%),</td>
</tr>
<tr>
<td>Pulmonary</td>
<td>Cough (30%), dyspnea (23%), sore throat (22%), hiccups (11%)</td>
</tr>
<tr>
<td>Gastrointestinal</td>
<td>Vomiting (68%), diarrhea (65%), anorexia (65%), abdominal pain (44%), dysphagia (33%), jaundice (10%)</td>
</tr>
<tr>
<td>Hematological</td>
<td>Any unexplained bleeding (19%), melena/hematochezia (14%), hematemesis (4%), vaginal bleeding (3%), gingival bleeding (2%), hemoptysis (2%), epistaxis (2%), bleeding at injection site (2%), hematuria (1%), petechiae/ecchymoses (1%)</td>
</tr>
<tr>
<td>Integumentary</td>
<td>Conjunctivitis (21%), rash (9%)</td>
</tr>
</tbody>
</table>

WHO Ebola Response team. NEJM 2014

**CCHF: Poor prognostic factors**

- Thrombocytopenia
- Leukocytosis
- Prolonged aPTT
- Decreased fibrinogen
- Elevated ALT, AST, LDH
- Hematemesis
- Melena
- Hematuria
- Diarrhoea
- Somnolence
- Splenomegaly

Independent predictors of mortality

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**Viral load is predictor of outcome**


**Special investigations**

- Haematology - FBC
  - Thick & Thin smear (REPEAT)
  - Coagulation (PT, aPTT)
- MCS - Blood/Fecal/Urine
- Biochemistry & LFT - U&E / Transaminases
- Malaria Ag test
- Imaging - CXR & Liver Ultrasound

**Diagnosis of VHF**

Critical information: Date of onset of fever/symptoms

- viremia
- IgM
- IgG
- days post onset of symptoms

Fever
RT-PCR
ELISA IgM
ELISA IgG

IgM, up to 3 – 6 months
IgG: 3 – 5 years or more (life-long persistence?)
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Real Time PCR
- Used to diagnose acute infection
- More sensitive than antigen detection ELISA
- Identification of specific viral genetic fragments
- Performed in select CLIA-certified laboratories

Differential diagnosis
- Other HFVs
  - Leptospirosis
  - Meningococcemia
  - Rickettsial diseases
  - Malaria
  - Sepsis
  - Influenza
  - Viral hepatitis
  - Toxic shock syndrome
- Idiopathic or thrombotic thrombocytopenic purpura
- Hemolytic uremic syndrome
- Acute leukemia
- Collagen-vascular diseases

68% of cases have an initial misdiagnosis of various diseases

Consider geographic distribution of diseases

Farrar J et al. Manson's Tropical Disease 2015

Not just Ebola; think other VHF

Moore LSP et al. British J Hospital Medicine 2014;75:515-20
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Ebola vs Malaria

Beyond malaria: causes of fever in outpatient Tanzanian children

Endocarditis


Endocarditis

Courtesy of Eskild Petersen
VHF: Treatment

- Standard treatment is supportive therapy
- Early aggressive intensive care support
- Support of coagulation system
- Careful monitoring
  - Oxygenisation
  - Fluid & electrolyte balance
  - Blood pressure
- Early use of inotropic agents (dobutamine)
- Ventilation support for severe cases
- Renal replacement therapy
- Pain management
- Parenteral nutrition

Support of coagulation system

- Thrombocyte suspension
  - Indicators: thrombocyte count, bleeding
- Fresh frozen plasma
  - Indicators: PT, aPTT
- Erythrocyte suspension
  - Indicator: Hb

Early recognition is critical

- Initiate
- Identify
- Diagnose
- Isolate
- Treat
- Inform

VHF risk assessment

Modified from Public Health England

Moore LSP et al. British J Hospital Medicine 2014;75:515-22

Isolation

Standard
Contact
Droplet

Isolation

Royal Free London NHS Foundation Trust
Cohorting

Personal protective equipment (PPE)

Conclusion

- Obtain a detailed travel history
- Assess risk factors for infection
- Early clinical assessment of the severity of infection is crucial
- Early diagnosis, early management and isolation of patient
- Inform ID & CM and public health
Leblebicioglu - Fever with haemorrhagic manifestations
CASE PRESENTATION

- Male 28 years old, without significant medical history
- Spent with his girlfriend 8 days in Malaysia (including a 2 day trip in Malaysian Borneo district for rafting)
- Residence in 5 star hotel, no consumption of non-commercial food or drinks
- No contact with animals or insects and good anti-mosquito protective measures
- Malaria prophylaxis with atovaquone proguanil
- Pre-travel consultation; a review of his personal record revealed effective vaccination against hepatitis B and A
- A small abrasion was noticed in his left foot during outdoor activities without evidence of infection
Poulakou - Seizures and coma in a traveller returning from the tropics

CASE PRESENTATION

- Day 3 of his return:
  - Mild symptoms of illness, fever 38.0°C, sore throat, headache
  - Treated with paracetamol, symptoms disappeared after 48 hours of bed rest
  - Resumed work on day 6 after his return
- On day 14, he develops new fever up to 39°C, malaise, myalgias, retinobilateral headache, vomiting, diarrhea and erythematous rash
- His girlfriend returns late after work and finds him unconscious
- On the way to the hospital he develops seizures

CASE PRESENTATION

- Dyspnoea, tachypnoea (RR 32/min)
- Hypo apa (SaO2 90%, FiO2 0.6)
- Bilateral Ronchi
- Oliguria
- Menigitis
- Glasgow coma scale 5
- Arterial blood gases: metabolic acidosis pH 7.29, base excess, − 6.1 mmol/L
- Arterial blood pressure 90/55 mmHg
- Electrocardiogram (ECG) showed sinus tachycardia (110bpm) with inferolateral T wave inversion
- Xray: bilateral alveolar –interstitial infiltrates, peripherally located in the right lung

CASE 2

ON HOSPITAL ADMISSION

- HT 30%
- HB 9.2mg/dL
- PLT 70,000/mm3
- WBC 13,000/mm3 (Poly 48%, Lympho 40%, Eo0.2%)
- Urea 120mg/dL
- Creatinine 4.8 mg/dL
- Gluc 95mg/dL
- ALT 1228 IU/L
- AST 2301 IU/L
- ALP 430 IU/L
- Gl 65 IU/L
- Tbl 14.1 mg/dL
- Dbl 10.9 mg/dL
- Urinalysis: granular casts, WBCs, protein ++
Q1: WHICH IS THE MOST PROBABLE DIAGNOSIS?

1. Malaria
2. Viral Encephalitis/meningitis
3. Typhoid fever
4. Rickettsial infection
5. Eosinophilic meningitis
6. All the above
7. Other

RELATIVE RISKS FOR TRAVELLERS

Risk | Illness
---|---
High | Malaria (all forms), typhoid, leptospirosis, dengue, chikungunya, arbovirus, cholera, meningitis, typhus, plague, rabies, yellow fever, Rift Valley fever, yellow fever, avian influenza
Moderate | Typhoid fever, malaria, yellow fever, scrub typhus, leishmaniasis, filariasis, malaria, meningitis, arbovirus, dengue, hanta virus, Q fever, plague, yellow fever, Rift Valley fever, yellow fever, avian influenza
Low | Malaria (all forms), typhoid, leptospirosis, dengue, chikungunya, arbovirus, cholera, meningitis, typhus, plague, rabies, yellow fever, Rift Valley fever, yellow fever, avian influenza
Very low | Typhoid fever, malaria, dengue, chikungunya, arbovirus, cholera, meningitis, typhus, plague, rabies, yellow fever, Rift Valley fever, yellow fever, avian influenza

Q2: WHAT FURTHER TESTS WOULD YOU ASK?

1. Brain MRI
2. Malaria testing
3. Serology for WNV, Chikungunya, Dengue, arboviruses, rickettsiae, leptospirosis, tuberculosis
4. All the above
5. Other
**CASE 2**

**ON ADMISSION**

Radiology
- U/S abdomen: mild hepatomegaly and splenomegaly
- Brain C/T: non significant

Lumbar puncture
- Lymphocytic pleocytosis (385 cells/mm³, lymphocytes 90%)
- Gluc: within normal range
- Protein slightly elevated
- PCR for bacterial pathogens: negative
- Gram stain and latex negative

**CASE PRESENTATION**

- Over the next 2 days, his condition deteriorated. He spiked high fevers, had tachycardia (heart rate, 120/min), was hypotensive (blood pressure, 80/64 mmHg), remained hypoxic (Po2, 71.9 mmHg; FiO2, 0.6), jaundiced (bilirubin, 18.5 mg/dL) and had progressive renal failure (creatinine, 6.1 mg/dL)

- On day three in the ICU
  - The white cell count was 16,400/mm³ and the platelet count dropped to 10,000/mm³
  - He became anuric (renal replacement treatment started), developed new seizures and ARDS
  - He developed rhabdomyolysis with creatinine phosphokinase (8037 IU/L [RR, 0–250 IU/L])

**TREATMENT**

- Fluids+inotropes
- Intubation/mechanical ventilation
- Artesunate+doxycycline iv
- Ceftriaxone
- Serial malaria smears
LABORATORY RESULTS

- Thick and thin blood films examined twice for malaria parasites were negative
- Blood cultures were negative
- Targeted testing was negative for:
  - Dengue fever (serology and PCR, blood and CSF)
  - CHIKV (serology)
  - WNV (serology and PCR, blood and CSF)
  - Leptospira (serology)
  - Rickettsia (serology)
  - Influenza viruses A and B (antibody, serology)
  - Adenovirus, Enterovirus (PCR)
  - Salmonella (serology)
  - Legionella (antibody, PCR)
  - Cytomegalovirus (serology, PCR)
  - Epstein–Barr virus (serology, PCR)
  - Toxoplasma (serology)
  - Legionella (urine antigen, serology)
  - Enterovirus (serology)

Q3: WHAT ARE YOUR THOUGHTS NOW?

1. Malaria
2. Viral Encephalitis
3. Rickettsial infection
4. Leptospirosis
5. All the above are still possible
6. Other

ED EVALUATION OF THE FEBRILE TRAVELER

1. What infections are **possible** given the patient’s travel history
2. What infections are **probable** given the patient’s medical history and presentation
3. What infections are life-threatening or contagious or both
PRE TRAVEL COUNSELLING - MALAYSIA

Malaria
Areas with malaria: Present in rural areas of Malaysian Borneo (Sabah and Sarawak Provinces) and to a lesser extent in urban areas of West Malaysia.
Estimated relative risk of malaria for US travelers: Low.
Drug resistance: Chloroquine.
Malaria species: P. falciparum (30%), P. vivax (50%), remainder P. Knowlesi, P. malariae, and P. ovale. P. Knowlesi has been reported to cause 28% of cases in Sarawak and is known to cause cases in both Malaysian Borneo and Peninsular Malaysia.
Recommended chemoprophylaxis: Atovaquone-proguanil, doxycycline, or mefloquine.

Yellow Fever
Requirements: Required if traveling from a country with risk of YFV transmission and ≥1 year of age, including transit >12 hours in an airport located in a country with risk of YFV transmission.
Other Vaccines to Consider: Routine, hepatitis A & B, typhoid, Japanese encephalitis, and rabies.

PRACTICAL APPROACH TO AN ILL TRAVELER
Travel history: date and places visited
Fever: duration, pattern Biphasic?
Potential exposures:
Travel to rural areas
Sexual exposure
Freshwater swimming
Climatic conditions, season
Ingestion of contaminated food
Insect or animal bites
Exposure to ill people or injuries
Vaccination history
Use of prophylactic medication and compliance
Use of protective equipment
Immune status

COMMONEST CAUSES OF FEVER IN RETURNING TRAVELLERS (%)

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>MacLean et al (n=587)</th>
<th>Doherty et al (n=195)</th>
<th>O'Brien et al (n=232)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Malaria</td>
<td>4</td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td>Hepatitis</td>
<td>6</td>
<td>11</td>
<td>3 (Hep A)</td>
</tr>
<tr>
<td>Respiratory infection</td>
<td>11</td>
<td>2</td>
<td>24</td>
</tr>
<tr>
<td>Uveitis</td>
<td>4</td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td>Dengue fever</td>
<td>4.5</td>
<td>5.1</td>
<td>14 (uncomplicated)</td>
</tr>
<tr>
<td>Gastroenteritis</td>
<td>2</td>
<td>3.5</td>
<td>3</td>
</tr>
<tr>
<td>Verse disease</td>
<td>0</td>
<td>1.5</td>
<td>3</td>
</tr>
<tr>
<td>Enterobacter</td>
<td>1</td>
<td>5</td>
<td>0.4</td>
</tr>
<tr>
<td>Brucellosis</td>
<td>1</td>
<td>3.5</td>
<td>2</td>
</tr>
<tr>
<td>Acute LVF infection</td>
<td>0.3</td>
<td>1.8</td>
<td>0.4</td>
</tr>
<tr>
<td>Nephritis</td>
<td>1</td>
<td>2</td>
<td>1</td>
</tr>
<tr>
<td>Other infections</td>
<td>4.3</td>
<td>9.2</td>
<td>9</td>
</tr>
<tr>
<td>Non-malarial fevers</td>
<td>16</td>
<td>28</td>
<td>19</td>
</tr>
</tbody>
</table>

Poulakou - Seizures and coma in a traveller returning from the tropics

**INCUBATION PERIODS**

<table>
<thead>
<tr>
<th>Pathogens Causing CNS Involvement in the Returned Traveller</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Short (&lt;10 days)</strong></td>
</tr>
<tr>
<td>- Viral haemorrhagic fevers</td>
</tr>
<tr>
<td>- Dengue fever</td>
</tr>
<tr>
<td>- Yellow fever</td>
</tr>
<tr>
<td>- Arboviral infections (including dengue and yellow fever)</td>
</tr>
<tr>
<td>- Bacterial meningitis</td>
</tr>
<tr>
<td><strong>Medium (11-21 days)</strong></td>
</tr>
<tr>
<td>- Malaria (particularly P falciparum)</td>
</tr>
<tr>
<td>- Typhoid fever</td>
</tr>
<tr>
<td>- Leptospirosis</td>
</tr>
<tr>
<td>- Rickettsioses: scrub typhus, spotted fever group, Q fever</td>
</tr>
<tr>
<td>- Brucellosis</td>
</tr>
<tr>
<td>- Enteroic protozoal infections</td>
</tr>
<tr>
<td>- Enteroic hepatitis</td>
</tr>
<tr>
<td>- Strongyloides</td>
</tr>
<tr>
<td>- Lyme</td>
</tr>
<tr>
<td>- African trypanosomias</td>
</tr>
<tr>
<td><strong>Long (&gt;30 days)</strong></td>
</tr>
<tr>
<td>- Malaria</td>
</tr>
<tr>
<td>- Viral hepatitis</td>
</tr>
<tr>
<td>- Schistosomias</td>
</tr>
<tr>
<td>- Tuberculosis</td>
</tr>
<tr>
<td>- Amoebic liver abscess</td>
</tr>
<tr>
<td>- Enteroic protozoal infections</td>
</tr>
<tr>
<td>- Enteroic hepatitis</td>
</tr>
<tr>
<td>- Strongyloides</td>
</tr>
<tr>
<td>- Lyme</td>
</tr>
<tr>
<td>- Rabies</td>
</tr>
<tr>
<td>- Leishmanias</td>
</tr>
<tr>
<td>- American trypanosomias</td>
</tr>
</tbody>
</table>

**PRACTICAL APPROACH TO AN ILL TRAVELER**

Physical examination
- Signs of meningism ✓
- Focal neurologic manifestations X
- Dermatologic manifestations ✓
- Involvement of other organ systems ✓

**DIFFERENTIAL DIAGNOSIS OF PHYSICAL FINDINGS FOR SOME TRAVEL DISEASES**

<table>
<thead>
<tr>
<th>Lymphadenopathy</th>
</tr>
</thead>
<tbody>
<tr>
<td>- Plague, HIV, rickettsioses, brucellosis, leishmaniasis, dengue, lymphogranuloma venereum, Lassa fever</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Hepatomegaly</th>
</tr>
</thead>
<tbody>
<tr>
<td>- Malaria, leishmaniasis, amoebic liver abscess, typhoid, hepatitis, leptospirosis</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Splenomegaly</th>
</tr>
</thead>
<tbody>
<tr>
<td>- Malaria, leishmaniasis, trypanosomiasis, typhoid, brucellosis, typhus, dengue</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Jaundice</th>
</tr>
</thead>
<tbody>
<tr>
<td>- Hepatitis, malaria, leptospirosis, relapsing fevers, cholelithiasis, pancreatitis</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Petechiae/ecchymosis</th>
</tr>
</thead>
<tbody>
<tr>
<td>- Meningohezaemia, yellow fever, dengue, rickettsioses, viral haemorrhagic fevers, envenoming, leptospirosis</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Nystagmus/diplopia</th>
</tr>
</thead>
<tbody>
<tr>
<td>- Rabies, botulimum poisoning, neurotoxic snakebite envenoming</td>
</tr>
</tbody>
</table>
Poulakou - Seizures and coma in a traveller returning from the tropics

PRACTICAL APPROACH TO AN ILL TRAVELER

Diagnosis
- Basic blood work (CBC, BMP, LFT, urinalysis, blood cultures)
- Thick and thin blood film
- Imaging studies (CT, MRI)
- Lumbar puncture
- Special tests (EEG)
- Serology and viral identification

BMP indicates basic metabolic panel; CBC, complete blood picture; EEG, electroencephalogram; LFT, liver function test

Han M, Neurologist. 2005 January ; 11(1): 30–44

Management
- Treat potential life-threatening complications
- Assess for neurologic emergencies (status epilepticus, stroke, spinal cord compression)
- Consider empiric broad-spectrum antibiotic, antiviral or antiparasitic coverage for very ill patients
- Consult tropical or travel medicine expert

VECTORS OF INFECTION AND PROPHYLACTIC MEASURES

<table>
<thead>
<tr>
<th>Vector</th>
<th>Potential Infection</th>
</tr>
</thead>
<tbody>
<tr>
<td>Insects</td>
<td></td>
</tr>
<tr>
<td>Mosquito</td>
<td>Malaria, arboviral encephalitides, VHF</td>
</tr>
<tr>
<td>Flea</td>
<td>Plague</td>
</tr>
<tr>
<td>Tick</td>
<td>Tick-borne encephalitis, Crimean hemorrhagic fever</td>
</tr>
<tr>
<td>Fly</td>
<td>African trypanosomiasis, leishmaniasis</td>
</tr>
<tr>
<td>Animals</td>
<td></td>
</tr>
<tr>
<td>Bites</td>
<td>Rabies</td>
</tr>
<tr>
<td>Excreta</td>
<td>Toxoplasmosis, leptospirosis</td>
</tr>
</tbody>
</table>
Poulakou - Seizures and coma in a traveller returning from the tropics

**VECTORS OF INFECTION AND PROPHYLACTIC MEASURES**

<table>
<thead>
<tr>
<th>Vector</th>
<th>Potential Infection</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ingestion</td>
<td>Neurocysticercosis, V00, anthrax</td>
</tr>
<tr>
<td>Contaminated water</td>
<td>Polysomites, cryptococcosis</td>
</tr>
<tr>
<td>Dirty products</td>
<td>Enteric fever, amebiasis, cysticercosis, strongyloidias</td>
</tr>
<tr>
<td>Poor sanitation</td>
<td></td>
</tr>
<tr>
<td>Direct contact</td>
<td>Meningococcal meningitis, viral infections, Lassa fever, Ebola, tuberculosis</td>
</tr>
<tr>
<td>Sick contact</td>
<td></td>
</tr>
<tr>
<td>Sexual contact</td>
<td></td>
</tr>
<tr>
<td>Fresh water sports</td>
<td>Schistosomiasis, leptospirosis, scaphocephalus stenostomiasis</td>
</tr>
<tr>
<td>Mud/dirt contact</td>
<td>Hook worm, leptospirosis, larvae migrants</td>
</tr>
</tbody>
</table>

**Infection** | **Chemoprophylaxis** | **Treatment** | **Vaccine**  
Yellow fever | None | Supportive | Live vaccine  
Japanese encephalitis | None | Supportive |  
Tick-borne encephalitis | None | Supportive | Inactivated whole virus  
Meningococcal meningitis | Rifampin or ciprofloxacin if exposed | Wound treatment, active and passive immunisation |  
Typhoid | Rifampin if exposed | Cefotaxime, benzylpenicillin | Quadrivalent A, C, Y, W135  
Polio | None | Supportive | IPV, HDCV, PCV, BOP  
Rabies | None | Supportive |  
Malaria | According to local epidemiology | Quinine, mefloquine,Fansidar, artemether, artesunate |  

**Parasite** | **Neurologic Effects** | **Neuroimaging Findings** | **Treatment**  
Chagas disease | Headache, cognitive changes, seizures, tremor, headache | Leukoaraiosis or multiple ring-enhancing lesions with surrounding edema |  
Schistosomiasis | Headache, weakness, seizures, cranial neuropathy | Gyms of various sizes, sometimes in granulocyte clusters, granulomas |  
Toxocariasis | Headache, fever, weakness, optic neuritis | Vasogenic edema with heterogeneous enhancing lesions, subarachnoid and subdural effusions resembling small-vessel vasculitis |  

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**CNS INVOLVEMENT AND FEVER AND THROMBOCYTOPENIA/PETECHIAES**

- Severe malaria
- Coma, lethargy, delirium, seizures, retinal haemorrhages
- Dengue Haemorrhagic Fever
- Leptospirosis, Rickettsial infections
- Mental Status changes, seizures
- Meningococcaemia,
- Yellow fever, viral haemorrhagic fevers,

Spira AM, Lancet. 2003; 361(9367):1459-48

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**Q4: IS DIAGNOSIS OF MALARIA EXCLUDED SO FAR?**

1. Yes
2. No

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**Q5: IS DIAGNOSIS OF LEPTOSPIROSIS EXCLUDED SO FAR?**

1. Yes
2. No
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**PITFALLS**

- Malaria (serial smears, lab experience, rapid diagnostic methods, PCR, *P. knowlesi* infection)
- Leptospirosis (no optimal testing method)
- IgM ELISA can aid but slow!
- Phase-specific diagnostic methods
- Rickettsia (fatal if not treated early, difficult to diagnose)
- Biphasic fever
- Dengue and leptospirosis

Spira AM. Lancet. 2003;361(9367):1459-69

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**CASE PRESENTATION**

- The patient succumbed on the 10th ICU day due to multiorgan failure
- Brain haemorrhage was demonstrated on MRI
- Haemorrhagic tracheal secretions developed
- Broad spectrum antibiotics had been added to cover nosocomial sepsis
- Fever never responded to treatment

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**TAKE HOME MESSAGE**

- Febrile patient with CNS involvement
  - EXCLUDE MALARIA
  - Dengue can be fatal, particularly in repeat infections (DHF)
  - Rickettsia/Leptospira
    - Can be fatal if not treated early
    - Difficult to diagnose

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**DIAGNOSIS**

- It was established with other diagnostic test(s)
- Autopsy tests from lungs, brain, heart and kidneys were in line

**Q6: WHICH TEST LED TO THE DIAGNOSIS?**

1. PCR and/or rapid test for malaria
2. Dark field urine microscopy and repeat serology/PCR for *Leptospira* spp
3. Repeat serology for Dengue fever
4. Other

**Q7: WHICH IS THE MOST PROBABLE DIAGNOSIS?**

1. Malaria
2. Dengue haemorrhagic fever
3. Leptospirosis
4. Other
In the next slides the diagnosis will be discussed.

THANK YOU