# Causes of Sepsis In Migrants from North Africa and Middle East



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## Definition of Migration - WHO

- WHO migration is omnipresent.
  - skill shortages,
  - demographic imbalances,
  - climate change,
  - economic and political crises,
  - disasters.
- 1 billion estimated number of worldwide immigrants (214 M international 740 M internal)
- Migration flows comprise a wide range of populations; workers, students, refugees..

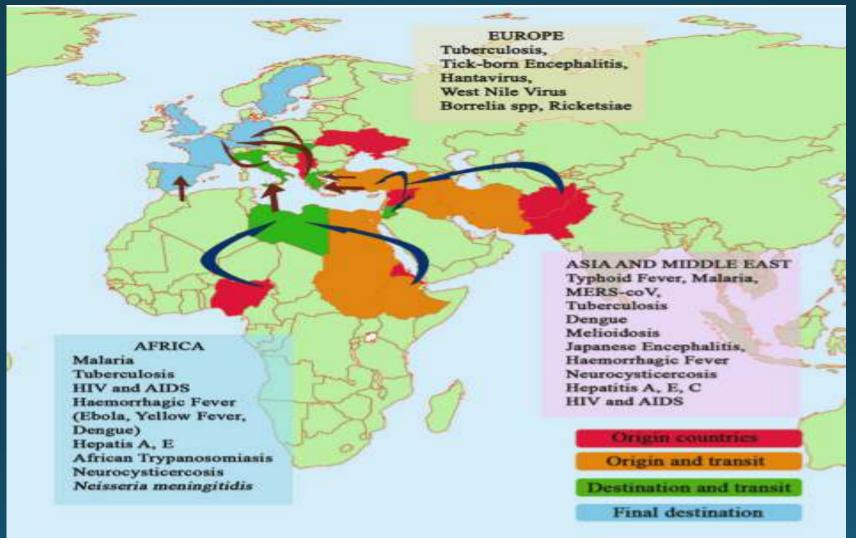
http://www.who.int/hac/techguidance/health\_of\_migrants/en/



#### Definition of The Problem

- Migratory influx N. African origin; today 6 M, 12–18 million by 2030.
- Syrian conflict: > 4 million persons are displaced.
- Turkey, Greece and Italy are currently the major portals of entries into the EU.
- The developed world is facing forgotten and now imported infectious diseases.
- Clinical spectrum is diverse, ranging from asymptomatic infection to severe septic shock.

#### Main Migration Roads & Risk For Infections



Critically ill migrants with infection: diagnostic considerations for intensive care physicians in Europe. Garyphallia Poulakou, Matteo Bassetti, Jean-François Timsit

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### Primary Evaluation of The Migrant Patient

- Important areas to ask about in fever in the returning traveler:
- Host Factors: past medical history, previous infections, diabetes, pregnancy, immunosuppression,
- Pre-travel Preparation: immunizations, malaria prophylaxis (type and compliance), protection (bed nets, repellents)
- Travel Itinerary: dates of travel, season of travel, destinations visited (regions, urban, rural), transportation, accommodation type



#### Primary Evaluation of The Migrant Patient

#### Exposure History:

- high-risk foods (local water, street food, uncooked meat),
- source of drinking water
- animal/insect exposure, bites,
- fresh water activities,
- blood and body fluid exposures (including sexual encounters, tattoos, IV drug use),
- sick contacts, health of fellow travelers.
- Likewise, the timing of the onset of symptoms, and any predispositions to infection should be noted.

emergencymedicinecases.com/fever-returning-traveler/



# Underlying Reasons of Infections in Migrants

- Inadequate shelter; living outdoors in the open,
- Crowding,
- Exposure to low temperatures,
- Low standards of environmental hygiene,
- Limited availability of potable water,
- Declining nutritional status,
- Interrupted immunization programs,
- Bariers to reach the primary health care



• 32 y/o, Syrian male, ED in Vienna, by ambulance with lethargy and difficulty in breathing.

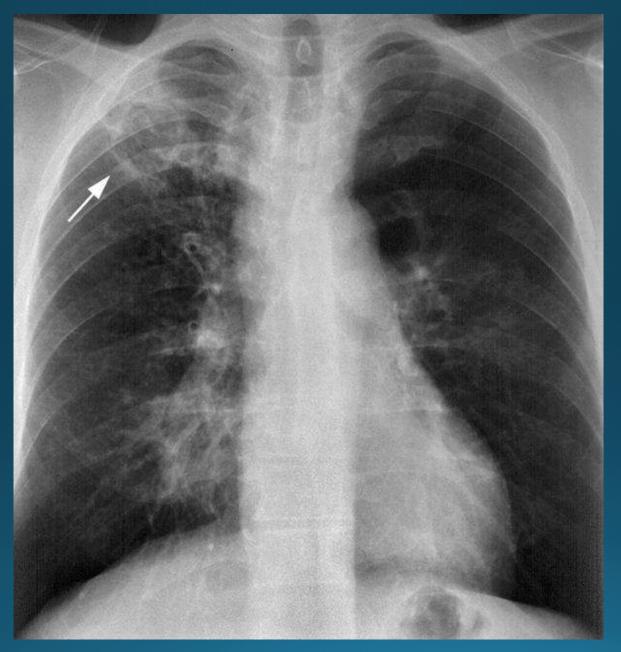
#### Vital Signs:

Temp 39.3°C, BP 110/60, HR 120 bpm, RR 32, O2 saturation 86% on a NRB.

#### • PE:

- Decreased LOC, only localizes to painful stimuli.
- No rashes, no neck stiffness, and no meningismus.
- Localized crackles-right upper and mid hemithorax.
- History:
- Arrived Vienna after 3 week journey mostly on foot.
- He had dry cough, malaise, fatigue, fever episodes by nights.





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#### **Tuberculosis**

- Facilitate TB infection/reactivation;
  - Malnutrition, poor living conditions, exhausted long trips and bariers to the health-care
- Primary infection: subtle & rare in healthy (2-3%)
  - In immuno-compromised patients, the primary infection may be rapidly progressive and fatal.
- The manifestations are similar to bacterial septic shock.
  - Survival is extremely poor, in hospital mortality rate of 79 %.
- Delay in the therapy is critical.



#### TB As A Source of Infection

#### **Pulmonary TB**

- Cavitary Pulmoner Lessions Endobronchial TB
- Pneumothorax Empyema due to TB and/ or bacterial superinfection
- Extensive pulmonary destruction

#### Miliary TB (more than 50% septic cases)

- GI TB peritonitis
- Renal Disease Pyelonephritis
- Genital origin epididymitis, orchitis, salpingitis
- Pott's Disease TB spondylitis
- TB pericarditis / endocarditis (very rare)
- Tuberculous Menindigitis



## Diagnosis & Management

- Acid-fast smears and cultures:
  - sputum, infected tissues and fluids or drainage (i.e; gastric aspirates, pleural fluid)
- PCR rapid and high sensitive
- Immediate Respiratory Isolation:
  - suspected patients should separated in waiting areas provided with surgical masks,
  - Health Care Workers: N95 masks (filter 1-µm particles with at least 95% efficiency)
  - CDC recommends: negative pressure rooms (at least 12 air changes per hour)
- Therapy: INH + rifampin + pyrazinamide + ethambutol





- A 35 year-old male, ED in Geneva, Italy, with multiple seizures.
- VS: Temp 40.1°C, BP 72/53, HR 114 bpm, RR 30, O2 Sat: 90%
- Initial glucose is 45 mg/dL.
- He receives 2 amps of D50W and 2mg of IV lorazepam.
- After 2 more doses of lorazepam the seizures stop.

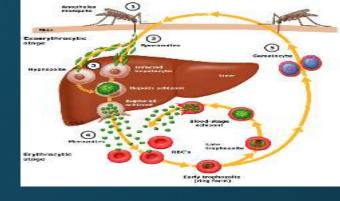
https://malariajournal.biomedcentral.com/articles/10.1186/1475-2875-10-378





- Phyical Examination:
  - He is diaphoretic, pale, he is confused, but following commands.
  - You palpate diffuse abdominal tenderness with no peritoneal signs and also a splenomegaly.
  - No signs of CNS enfection and no rashes are observed.
- History: He is a shipman returned from the voyage from Australia two weeks ago.
- You learned the only stop of the ship was Aden, Yemen, one month ago.

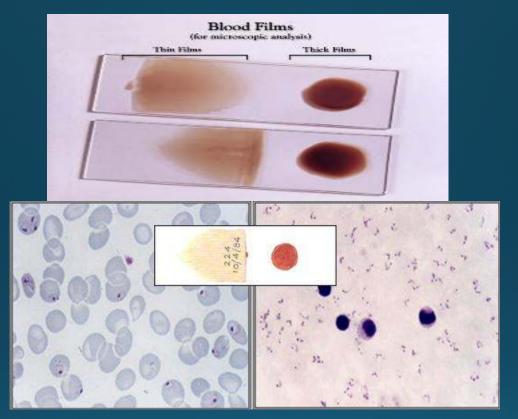
#### Malaria



- Vector: infected female Anopheles
- P. falciparum highest risk for septic shock, most infections occurs *month* after exposure.
- P. vivax and P. knowlesi can also cause fatal disease.
- Symptoms onset: rupture of schizont-containing erythrocytes - triggers an array of host cytokine responses
- Any patient with severe sepsis who just returned from a malaria endemic area should be tested for malaria promptly.



#### Thick/Thin Smear With Giemsa Stain



Gold standart - The first may be smear is positive in >90% of cases. Clinical suspicion: repeat smears every 12 hours until there are three negative smears to rule out Malaria.

PCR: detect parasite DNA are more sensitive, limited to reference laboratories.

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#### Manifestations of Severe Malaria

- Result of microembolisms originate from the parasitized (and non-parasitized) RBCs
  - (small infarcts, capillary leakage, and organ dysfunction)
- 1. Altered MS with or without seizures (GCS<11)
- 2. Prostration (Generalized weakness a person becomes unable to sit, stand, or walk without assistance)
- 3. Multipl convulsions: > 2 episodes within 24 hours
- 4. Respiratory distress or ARDS
- 5. Circulatory collapse Shock (BP< 80 mmHg)
- 6. Metabolic Acidosis (BE>8 mEq/L;HCO3<15)

Source: World Health Organization. Guidelines for the treatment of malaria, 3rd ed. WHO: Geneva 2015.

#### Manifestations of Severe Malaria

- 7. Renal failure: Cr>3mg/dL or urea>20mmol/L; Hemoglobinuria ("blackwater fever")
- 8. Hepatic failure:
  - Hypoglycemia (<40 mg/dL)</li>
  - Jaundice Bilirubin >3 mg/dL
  - Coagulopathy with or without DIC
- 9. Severe anemia or massive intravascular hemolysis
  - (<7 g/dL with parasite count >10,000/mcL (0.2 % parasitemia)
- 10. Hyperparasitemia: P. falciparum >10 % (>500,000/mcL)
  - \* One or more of the above

Therapy: Arthemisin derivates / quinidine + doxycycline

Source: World Health Organization. Guidelines for the treatment of malaria, 3rd ed. WHO: Geneva 2015.



- •28 y/o male, born in Morocco, resident of Madrid for 5 years.
- He made short trips several times to Morocco.
- He complains high fever and malaise, for 7-8 days.
- PM History: No foci for infection, no risk factors for HIV.
- Vital Signs: BP: 114/46 mmHg, Temp 38.9 °C, oxygen Sat 95%



- •PE: He is in good condition. No skin lesions and signs of meningeal irritation.
- Head and neck: Laterocervical small painfull
   LAP
- Abdomen: Hepatomegaly 8-10 cm in costal right shoulder and splenomegaly 16-18 cm in the left upper quadrant left costal margin.
- The rest of PE reveals as normal.
- Lab: 1.400 WBC N 54%, L 24%, M 20%, Hb 8.3 g/dl, Plt: 107.000/l



- Routine Lab and coagulation tests: Normal
- CXR: Normal.
- Study peripheral blood: Anisocitosis, no schistocytes / or poiquilocitos, abundant cytoplasmic toxic granulations.
- Serology: HIV, EBV, CMV, HAV, HBV and HCV negative.
- Mantoux: Negative.



Abdominal CT image - at renal level: Splenomegaly, giant homogeneous - 25 cm, Moderate hepatomegaly, retroperitoneal lymphadenopathy multiple.



#### Gargantilla Madera P, Pintor Holguín E.

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Semergen. 2016;xxx(xx):xxx-xxx



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www.elsevier.es/semergen



#### CARTA CLÍNICA

#### Leishmaniasis visceral en inmigrante marroquí

Visceral leishmaniasis in a morroccan immigrant

#### Introducción

La leishmaniasis es una infección producida por diversas especies del género Leishmania, que se transmite por la picadura de hembras de mosca pertenecientes al género Phlebotomus.

En nuestro país, la leishmaniasis es una zoonosis que afecta principalmente al perro (reservorio) y al hombre. Aunque es una enfermedad muy prevalente en Latinoamérica y otros países tropicales, la incidencia en la cuenca mediterránea no es nada desdeñable. Hay 3 síndromes clí-

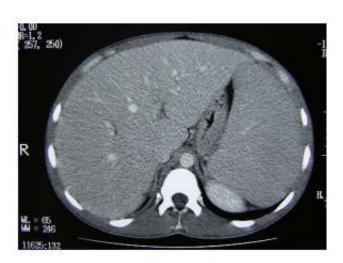


Figura 1 Imagen TAC abdominal: se objetiva una muy importante hepatoesplenomegalia sin lesiones ocupantes de espacio.

- Leishmania donovani serology (IFI IgG + was made 1/64)
- Biopsy: iliac crest, objectified amastigote forms of the parasite.
- Treatment with liposomal amphotericin B, remaining the apyretic patient from the first 48 h



#### Visceral Leismaniasis

- Intracellular protozoan L. donovani & L. infantum
  - Transmitted by Lutzomyia or Phlebotomus sandflies.
  - Sporadically in rural Africa, Asia, the Mediterranean basin.
- Mostly asymptomatic; in immunosupression the disease can reactivate.
- Definitive Diagnosis:
  - demonstration of parasite visualization of (amastigotes)
- Tests:
  - PCR: high sensitive
  - ELISA: recom. kinesin Ag (rK39) high sensitive
  - Indirect fluorescent antibody (IFA) > 1/64



#### Visceral Leishmaniasis

- Kala-azar "black fever"
- Nearly always lethal without treatment.
- Incubation: 2-6 months (few weeks to several years)
- The Pentad: fever, weight loss, hepatosplenomegaly, pancytopenia, and hypergammaglobulinemia.
- Pathophysiology:
  - L. invade and replicate in host macrophages; replicates in RES (marrow,spleen& liver)
  - Pancytopenia & hypergammaglobulinemia
- Immunosuppression increases risk for secondary bacterial infections. (TB, Pneumonia ..)

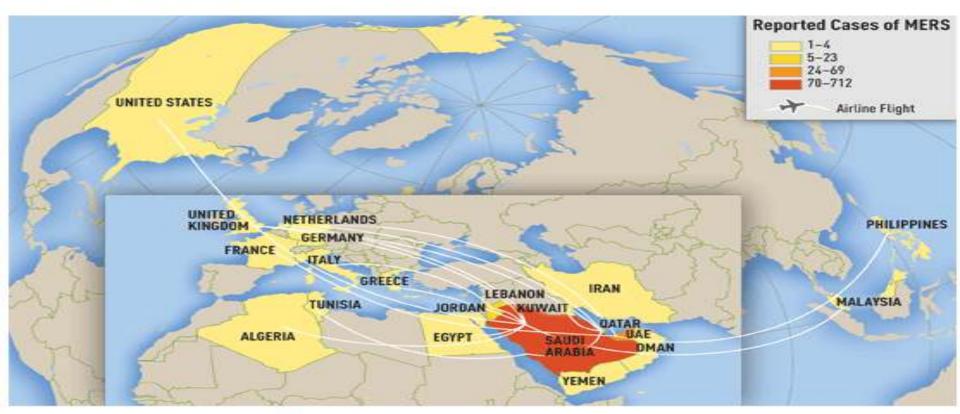


- 64 y/o woman, returned from Hajj to Istanbul
- She sufferred from fever, chills/rigors, headache, non-productive cough and shortness of breath, for last two days.
- Vital Signs: 94/48 BP, pulse 114 bpm, RR: 30/min, Temp 38.9 C, Sat O2: 84 %
- Details of History: Her husband sufferres same complains



## 2014 – MERS Distribution

Map 1-01. Distribution of confirmed cases of Middle East Respiratory Syndrome by reporting country<sup>1</sup>



PDF Version (printable)

<sup>&</sup>lt;sup>1</sup>Adapted from Figure 2 in: European Centre for Disease Prevention and Control. Epidemiological update: Middle East respiratory syndrome coronavirus (MERS-CoV). 5 Nov 2014 [cited 12 Nov 2014]. Available from:

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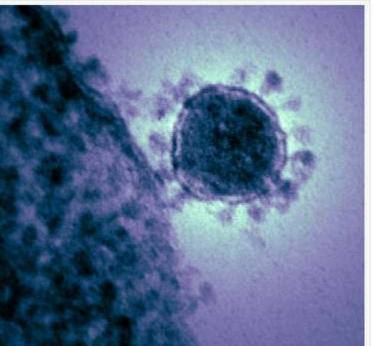
Outbreak News Radio

Europe » Austria reports 2nd imported MERS case

#### Austria reports 2nd imported MERS case

Posted by Robert Herriman on September 12, 2016 // 1 Comment

The Austria Ministry of Health reported on the second imported case of Middle East Respiratory Syndrome coronavirus (MERS-CoV), according to a news release (computer translated).



The previous imported case was reported in 2014.

According to local media reports (computer translated), the patient is a 67-year-old tourist from Saudi Arabia. He was diagnosed in Salzburg province and is currently hospitalized, according to the Salzburg government (computer translated).

According to the World Health Organization (WHO), since September 2012, they have been notified of 1,800 laboratory-confirmed cases of infection with MERS-CoV, including 640 deaths. The viral infection has been reported from 27 countries to date

The clinical spectrum of MERS-CoV infection ranges from no symptoms (asymptomatic) or mild respiratory symptoms to severe acute respiratory

## MIDDLE EAST RESPIRATORY SYNDROME - MERS

- September 2012-February 2014, total of 182 cases with 79 deaths.
  - Case fatality: 35 % (for SARS 11%)
- Beta-Coronavirus Like SARS,
- Incubation Prd: 5 days (2-14)
- Transmission: Droplet infection not certain, close contact
- Clinical spectrum: ranging from asymptomatic infection - ARDS, septic shock and death.



#### Possible Case & Definitive Case

- Patients who develop a fever and has severe respiratory failure and/or has infiltrations on CXR
  - AND traveled within 14 days to the countries in or near the Arabian Peninsula\*
  - OR have a close contact with an ill traveler (symptomatic) traveled within 14 days to to the countries in or near the Arabian Peninsula
- \*KSA, UAE, Oman, Jordan, Kuwait, Yemen, Lebanon & Iran
- Close contact: (without PPE)
- being within approximately 2 m within the room or care area



## ED Management

- Airborne precautions: Healthcare workers PPE
  - including gloves,
  - long-sleeved gowns,
  - eye protection and
  - particulate respirators (N95 or equivalent).
- Airborne Infection Isolation Room (AIIR):
  - negative pressure; high-efficiency particulate air (HEPA) filter
- PCR can be used to detect MERS-CoV serial collection of respiratory specimens
- Supportive & ICU Care: No current immunization



#### Ebola Virus Disease

Severe, often fatal disease in humans.

Transmitted to people from wild animals and it spreads in the human population; by close contact with;

the blood, secretions, organs or other bodily fluids of infected people and animals.

Difficult to distinguish from other exotic infections,

but having traveled to a country (e.g. recently to Central and West Africa) is a risk to be tested.



## Symptoms of Ebola

- Diagnosing infected person for only a few days is difficult. The early symptoms, are nonspecific.
- Fever
- Severe headache
- Muscle pain
- Weakness
- Fatigue
- Diarrhea
- Vomiting
- Abdominal (stomach) pain
- Unexplained hemorrhage (bleeding or bruising)

Symptoms may appear anywhere from 2 to 21 days after exposure to Ebola, but the average is 8 to 10 days.



### Treatment

- Diagnosis PCR & ELISA
- No FDA-approved vaccine or medicine (e.g., antiviral drug) is available.
- Symptom based treatment is main practice.
  - Provide IV and balancing electrolytes.
  - Maintain oxygen status and blood pressure.
  - Treat other infections if they occur.
- Recovery depends on good supportive care and the patient's immune response.



## Hemorrhagic Fevers Crimmean-Congo Hemorrhagic Fever

- Tickborne viral disease common the Middle East especially in Turkey.
- Mortality: 3-30%.; sudden onset of fever & symptoms
- Hemorrhagic period: develops rapidly on 3rd-5th days
  - Thrombocytopenia, PT and aPTT can be prolonged.
  - Leukopenia and elevated liver enzymes, LDH, Cr.
- Diagnosis : Clinical + Serology.
- Treatment: supportive, treat coagulopathy, IV ribavirin.



# Hemorrhagic Fevers Dengue

Source: CDC – YellowBook 2016 & HealthMap



- Endemic in Latin America, the Caribbean, Southeast Asia.
- Risk: in Sudan & Yemen
- Killed 27 people 3000 cases
  - in outbreak Yemen Shawba province in June 2016
  - 3000 new cases reported in 2016 in KSA
- Dengue Hemoorhagic Fever + Shock may be fatal
- Early therapy mortality reduces from 10% to <1 %.</li>
  - No antiviral agents; no chemoprophylaxis & vaccines exist for dengue.
  - Closely monitor in ICU; replacement of severe fluid leakage

# Miscellaneous Possible Causes for Sepsis In Migrants

- Respiratory disease: Viral bacteria
- GI infections: Typhoid fever complications
- GU Infections: Abortus (non-hygenic) & miscariages
- CNS: N. Menendigitis crowded living
- Soft tissue infection: fasciitis due to trauma / frostbite etc..
- Zoonozis Rabies
- Tick born diseases mediterranean spotted fever (Rickettsia conorii)
- Liver abcess: amoebic, cyst hydaticus (Ecchinococci)

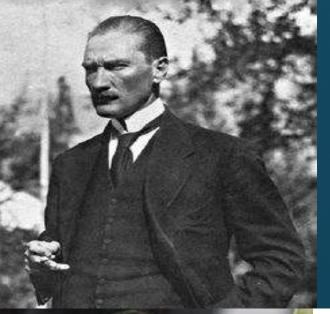


## Take Home Messages

- Fever + travel / migrant history → Red flag
- Detailed anemnesis:
  - travel itenary, vaccines, comorbities, duration of the symptoms etc.
- Start appropiate theraphy early (falciaparum malaria, TB etc)
- Managed shock early antibiotherapy
- Isolation as soon as possible if needed.
- Inform local public health authorities.

Thank you for your attention...





#### Peace at home, peace at the world.

Mustafa Kemal Atatürk

Founder of Republic of TURKEY





