FEVER IN THE RETURNED TRAVELER
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OBJECTIVES
- Develop a differential diagnosis and workup plan for fever in returning travelers.
- Take an adequate travel history.
- Plan the management for common febrile illnesses present in travelers.

EPIDEMIOLOGY
- Estimated 1.9M US children travel internationally each year
- 20-70% (of all travelers) report some illness associated with travel
- ~5% report fever
- 50% of travelers to developing countries will have a health problem during/after trip
- 14% seek medical care
- 5% hospitalized
- 1 in 100K will die

TRAVEL HISTORY
- Travel dates
- Geographic locations visited (rural vs urban)
  - Including locations passed through/airport layovers
- Pre-travel immunizations
- Chemoprophylaxis during travel
- Nature of trip – tourist, or visiting friends & relatives
- Accommodations (tent, dorm, household, hotel)
- Activity-based risk factors
  - Insect bites, contact with animals, freshwater exposure, soil exposure, sexual contact, needle exposure
- Foods and beverages

INCUBATION PERIODS
- Time since beginning of trip
- Antimicrobial medications can extend typical incubation period
- Brief (<14 days)
- Medium: 14 days to 6 weeks
- Long (>6 weeks)

DIAGNOSTIC TESTS
- Focus first on life-threatening diseases
- Blood cultures
- Peripheral blood smears
- Basic labs – CBC, CMP, UA, U/C, stool studies
- Store a tube of serum for future paired (acute vs convalescent) serologic tests
DIFFERENTIAL DIAGNOSIS

- Common things are common
  - Undifferentiated fever
  - Malaria, Dengue, Typhoid, Rickettsial diseases, Leptospirosis

- Different resistance patterns abroad
  - Dengue Hemorrhagic Fever, Lassa fever, Ebola, Yellow Fever
  - Respiratory infections
    - Legionnaire disease, Tuberculosis, non-tuberculous mycobacteria, Q fever

- Eosinophilia + fever
  - "worms, wheezes, weird diseases" – hookworm, ascaris, Strongyloides, echinococcosis, Barnea, schistosomiasis
  - Chagas, onchocerciasis

- East African trypanosomiasis, oral mononucleosis, Nile, malaria, African, reptilian diseases, leprosy

MALARIA

- Most common "exotic" disease in returned traveler
- 2.7M deaths/year
- 75% of these in African children
- Protozoal infection – Plasmodium genus
  - P. falciparum (90%), P. vivax, P. ovale, P. malariae
  - Vector – Anopheles mosquito

- Treatable & deadly – high index of suspicion
  - Fever, chills, vomiting, melena, headache, splenomegaly

- Common presentations – variable presentation
  - 48- or 72-hour periodic fever only in ~1/3 patients
  - Most kids have daily fevers; half will be afebrile at time of presentation

- Don't trust chemoprophylaxis

MALARIA – DIAGNOSIS

- Thick & thin peripheral blood smear with Giemsa stain
  - Thick smear 10x more sensitive
  - This smear for speculate & load

- If high suspicion for malaria, repeat smear – qfi for at least 3 negative sets to rule out
  - Thrombocytopenia without leukocytosis

- Alternatives:
  - Rapid antigen detection tests – available outside the US
  - PCR – government-sponsored labs

MALARIA – TREATMENT

- Falciparum malaria can rapidly progress
- If malaria diagnosed or suspected, admit patient
  - IV for hyperparasitemia (>2% infected RBC in travelers, >10% in children who emigrated from endemic areas)
  - Chloroquine resistant vs sensitive
    - History important – area visited, chemoprophylaxis
    - IV quinidine or quinine
    - Monitor for QT interval prolongation, hypoglycemia & hypoglycemia

- Reportable disease to CDC

Figure 13 Countries endemic for malaria in 2000 and 2016. Countries with 3 consecutive years of zero indigenous cases are considered to have eliminated malaria. No country in the WHO European region reported indigenous cases in 2016 but Tajikistan has not had 3 consecutive years of zero indigenous cases. Its last case being reported in July 2016. Source: WHO 2018 report
**DENGUE FEVER**
- Flavivirus transmitted by Aedes aegypti and A. albopictus mosquitoes.
- Tropic & subtropic regions.
- ~7% of febrile patients with recent travel to endemic area.
- Incubation period 4-7 days.
- Symptoms range from mild flu-like illness to severe muscle pain ("breakbone fever").
- Duration 5-7 days.
- Maculopapular rash near time of defervescence.

**DENGUE HEMORRHAGIC FEVER**
- Rare in travelers.
- Result of antibody-dependent enhancement/overstimulation (requires prior infection).
- Can progress to circulatory failure and dengue shock syndrome in 20-30% of patients.
- Symptoms: High fever, hepatomegaly, bleeding from mucosa, GI, injection sites, petechiae, purpura.
- Diagnosis: Thrombocytopenia and hemoconcentration (rise in Hct of >20% for age).
- Plus fever plus any hemorrhagic sx = DHF (per WHO).
- May also see elevated LFTs, albuminuria.
- Compare serum antibody titers from acute and convalescent phases.
- Treatment: Supportive care (fluid, blood products).
- Avoid NSAIDs due to platelet function inhibition.

**RIKETTSIAL DISEASE**
- (Possibly) 3rd most important cause of acute febrile illness in travelers.
- 2 groups – typhus & spotted fever.
- Good news – similar presentation, similar treatments.
- Classic triad: Travel history, fever, rash.
- Often no history of tick bite.
- 1-2 week incubation period.
- Spotted fever group – "Tick borne typhus.
- Worldwide distribution.
- Rocky Mountain Spotted Fever, Mediterranean spotted fever, rickettsialpox.
- RMSF most virulent – Rickettsia rickettsii.
- DIC, acute renal failure, death.
- Most common in travelers, less severe disease.
- Diagnosis: Serologic antibody testing. May see thrombocytopenia.
- Treatment: Doxycycline (even under 9yo).

**TYPHOID/PARATYPHOID FEVERS**
- Indian subcontinent, Philippines, Latin America.
- Fecal-oral transmission of Salmonella typhi or S. paratyphi (no animal reservoir).
- 5-21 day incubation period.
- Symptoms: fever, chills, headache, anorexia, nausea, malaise, rose spots.
- Constipation in older children & adults, diarrhea in infants.
- Milder clinical course in kids <2 years.
- Diagnosis: Blood & stool cultures (bone marrow – most sensitive).
- Leukopenia, anemia, thrombocytopenia.
- Elevated LFTs.
- Treatment: 3rd generation cephalosporin for 7-14 days.
- Fluoroquinolones in adults.

**LEPTOSPIROSIS**
- Leptospira interrogans, harbored in asymptomatic animals (rodents), transmitted in urine (direct contact or contaminated water).
- Global presence but more common in tropics.
- Freshwater sports, farmers.
- 10 day incubation period.
- Mild form – Non-specific symptoms.
- Modest, acute febrile illness
- Conjunctival chemosis without discharge, aseptic meningitis, pulmonary involvement.
- 5-7% mortality.
- Thought to be immune-mediated.
- Diagnosis: Microscopic agglutination test with 4x rise in antibody titers.
- Treatment: Antibiotics recommended; most cases resolve spontaneously.
- Broad-spectrum antibiotics sometimes used.

**VIRAL HEMORRHAGIC FEVERS**
- Rare, but scary.
- Present similarly – fever & flu-like symptoms (headache, myalgia, rash, GI sx).
- Arboviruses.
- Yellow fever (3-6 day incubation) 3 classic phases.
- Mild flu-like sx
- Remission (no sx) for 1 day
- Icterus, hemorrhage, AMS, shock (day 3-4).
- Dengue hemorrhagic fever.
- Lassa fever (3-21 day incubation) – more gradual onset.
- Filoviruses.
- Ebola, Marburg.
- Treatment – supportive.
- Ribavirin in Lassa.
SUMMARY

- Travel history is KEY
- Locations, dates, exposures
- Common things are common...but don't forget about malaria
- "Exotic" illness frequently have missed/delayed diagnosis
- Systems evaluation
- Supportive care & empiric therapy if ill

REFERENCES

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