DIFFERENTIAL DIAGNOSTICS OF FEVER FROM TROPICS AND SUBTROPICS

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5th year, Tropical Medicine

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INVESTIGATION AFTER RETURNING FROM TROPICS

• MEDICAL HISTORY
  – Travel history
  – Incubation period can be months to years

• PHYSICAL EXAMINATION
  – Check focal signs and symptoms

• FIRST LINE LABORATORY INVESTIGATIONS
  – WBC and differential counts, thick and thin blood smears, BC

• SPECIAL LABORATORY INVESTIGATIONS
  – Serology, cultivation, PCR

• IMAGING METHODS
  – X-ray, ultrasound, CT, NMR, echocardiography

• OTHER CONSILIARY EXAMINATIONS
  – Pulmonary, dermatology, ENT, surgery
MEDICAL HISTORY

• TRAVEL HISTORY: (chronology)
  – Visited countries, season
  – Rural regions, overnight staying, swimming in rivers and seas, fresh water
  – Mosquitoes, ticks, flys, flies, lice biting
  – Spider, scorpion, snail, dog, cat, monkey biting
  – Contact with animals: dogs, cats, parrots, rodents, animal skin
• PROPHYLAXIS: Travel vaccination, antimalarials, repelents, mosquito nets, insecticides, sun lotions
• DRUGS: antibiotics, antimalarials, analgetics, infusions, blood transfusions
• DIETE: water, fruits, etc.
• SEXUAL CONTACTS
• ALERGY: season, antibiotics, food, polen, animals
• MEDICAL PROBLEMS: nausea, vomiting, diarrhea, fever
• PROFESSION
• FAMILY HISTORY: sicle cell disease, tuberculosis
CLINICAL AND LABORATORY EXAMINATION IN PATIENTS WITH FEVER AFTER RETURNING FROM TROPICS

MEDICAL EXAMINATION
MEDICAL HISTORY

BASIC LABORATORY EXAM.: • Thick and thin blood film • Blood culture • Blood count & differential count • FW, CRP, Quick, PCT

OTHER LABORATORY & IMAGING EXAM.

SPECIAL LAB. EXAM IDENTIFICATION OF ETIOLOG. AGENTS

SEROLOGY CULTURE Ag DETECTION MOLEC.METHODS
PHYSICAL EXAMINATION

- **SKIN**
  - exanthema, hemorhagia, icterus, edema
- **EYE**
  - icterus, anemia
- **LYMPHNODES**
  - local, generalised lymphadenopathy
- **MENINGEAL SIGNS**
  - headache, vomiting, tremor
- **THROAT**
  - pharyngitis, streptococcal tonsillitis
- **CHEST**
  - Bronchitic signs, pneumonia
- **HEPATOMEGALY, SPLENOmegaly**
INCUBATION PERIOD

• SHORT (< 10 days):
  – Arboviral infections
  – Rickettsioses
  – Relapsing fever
  – Bacillary dysentery
  – Plaque

• MEDIUM (10–21 days):
  – Typhoid fever
  – Malaria (P. falciparum)
  – Leptospirosis
  – HIV infection
  – Brucellosis
  – Trypanosomiasis

• LONG (> 21 days):
  – Viral hepatitis
  – Malaria (P. falciparum also)
  – Amebiasis
  – Visceral leishmaniasis
  – Acute schistosomiasis
  – Filarial fever

• VERY LONG:
  (months – years)
  – Visceral leishmaniasis
  – Tertian malaria – relapses-
    P. vivax, P. ovale
  – Amebiasis – liver abscess
  – Chronic schistosomiasis
  – Hydatidosis, cysticercosis
INFECTIONS WITH LIMITED GEOGRAFICAL DISTRIBUTION

• Babesiosis  - N.E. USA (*B. microti*)
• Bartonellosis - Peru, Bolivia, Kolumbia, Equador
• Ebola - central Africa
• Ehrlichiosis  - N.E., M.W. USA (HGA); S.E..USA (HME)
• Hantaviruses - Europe, Far East (HF with renal syndrome)
               - Central, S. America (HF with pulmonary sy)
• Lassa - West Africa
• Leprosy  - India, Ethiopia, Bolivia
• Melllioidosis - S.E. Asia
• Loasis - West and Central Africa
• Onchocercosis - tropical Africa, South and Central America
• Trypanosomiasis - african: West, Central and East Africa
               - american: South and Central America
• Yellow fever - tropical Africa and South America
INFECTIONS DISTRIBUTED IN MOST PARTS OF TROPICS A SUBTROPICS

- Malaria
- Amebiasis
- Leishmaniasis (except S.E. Asia, S. Africa)
- Schistosomiasis (except India, Central America)
- Filariasis
- Tuberculosis
- Typhoid and paratyphoid fever
- Shigellosis, salmonellosis
- Viral hepatitis
- Dengue (rare in Subsaharan Africa)
- Rickettsiosis
- Endemic relapsing fever
CLINICAL AND LABORATORY EXAMINATION IN PATIENTS WITH FEVER AFTER RETURNING FROM TROPICS

MEDICAL EXAMINATION

MEDICAL HISTORY

BASIC LABORATORY EXAM.:  
- Thick and thin blood film  
- Blood culture  
- Blood count & differential count  
- FW, CRP, Quick,PCT

OTHER LABORATORY & IMAGING EXAM.

SPECIAL LAB. EXAM IDENTIFICATION OF ETIOLOG. AGENTS

SEROLOGY CULTURE Ag DETECTION MOLEC.METHODS
FEVER DIAGNOSTICS
Thick and thin blood smears

Unstained thick and thin blood smears
FEVER DIAGNOSTICS

Thick and thin blood smears (Giemsa-Romanowski staining)
MALARIA DIAGNOSTICS – BLOOD SMEARS

• Smears, both thick and thin blood films, are made from periferal blood, anytime in the regular intervals (every 12 – 24 hours) if malaria is suspicious, even if patient is without fever
  – In afebrile periode usually positive in: malaria, babesiosis, filarioses
  – In afebrile periode usually negative in relapsing fever and trypanosomiasis

• Thick smear is not fixed, thin smear is fixed with methanol (for 5 min) and both are stained after with Giemsa-Romanowski (20-30 min)

• The examination is repeated if negative minimum 3 – 4 times to exclude infection
DIAGNOSTICS OF MALARIA

• Blood smears are „golden standard“ in malaria diagnostics

• **Sensitivity** of the thick blood film: 50/μl ~ 0,001% parasitaemia (PCR sensitivity is 10-times higher)

• If smears are positive for malaria
  – species and stage are determined
  – parasitaemia is calculated
  – treatment with antimalarials is started immediately
  – smears are repeated every 12-24 h and parasitaemia is calculated to check the effect of antimalarials
MALARIA – DIAGNOSTICS III

Plasmodium falciparum – thin blood smear

Plasmodium falciparum – thick blood smear
BLOOD SMEARS - INTRACELULAR

MALARIA

*P. falciparum* gametocyte

*Plasmodium vivax* - trophozoites
BLOOD SMEARS - INTRACELULAR

BABESIOSIS

Babesia microti

Babesia bigemina

Babesia canis
BLOOD SMEARS - EXTRACELULAR

TRYPANOSOMIASIS

AFRICAN

Trypanosoma brucei

AMERICAN

Trypanosoma cruzi
BLOOD SMEARS - EXTRACELULAR

RELAPSING FEVER

EPIDEMIC

ENDEMIC

*Borrelia recurrentis*

*Borrelia sp.*
BLOOD SMEARS - EXTRACELULAR

FILARIOSIS

Loa loa

Wuchhereria bancrofti
BLOOD SMEARS

POSITIVE:
- Malaria
- Babesiosis
- Trypanosomiasis
- Filariosis
- Relapsing fever
- Bartonellosis
- Anaplasmosis, ehrlichiosis

NEGATIVE:
- Leishmaniasis
  - Buffy coat in HIV+
- Toxoplasmosis
- Amebiasis
- Schistosomiasis
POSITIVE BONE MARROW SMEARS
PERIFERAL BLOOD NEGATIVE

• Visceral leishmaniasis
• Histoplasmosis
• Lepromatous leprosy

*Leishmania infantum*

*Mycobacterium leprae* in the skin

*Histoplasma capsulatum*
LABORATORY INVESTIGATIONS IN FEVER DISEASES

FIRST LINE INVESTIGATIONS:

• Thin and thick blood smears
• Blood cultures (for aerobic and anaerobic bacteria)
• Total and differential white cell counts (WCC) FW, CRP, PCT
POSITIVE BLOOD CULTURES

- Bacterial sepsis, meningococcal infection
- Purulent (bacterial) meningitis
- Infectious endocarditis
- Typhoid and paratyphoid fever
- Plague, brucellosis, tularemia
- Pyogenic (bacterial) liver abscesses
- Bacterial focal infections
  - pneumonia 20 – 30 %
  - pyelonephritis 40 %
  - cholangitis 60 %
- Systemic mycotic infections

BLOOD CULTURES ARE NEGATIVE IN PARASITIC INFECTIONS
CLINICAL AND LABORATORY EXAM AT PATIENTS WITH FEVER AFTER RETURNING FROM TROPICS

MEDICAL EXAMINATION
MEDICAL HISTORY

BASIC LABORATORY EXAM.:  
• Thick and thin blood film  
• Blood culture  
• Blood count & differential count  
• FW, CRP, Quick, PCT

OTHER LABORATORY & IMAGINAL EXAM.

SPECIAL LAB. EXAM IDENTIFICATION OF ETIOLOG. AGENTS

SEROLOGY CULTURE Ag DETECTION MOLEC.METHODS
DIFFERENTIAL DIAGNOSIS OF ACUTE FEVER

<table>
<thead>
<tr>
<th>POLYMORPHONUCLEARS INCREASED</th>
<th>PMF NOT INCREASED</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Focal symptoms</strong></td>
<td><strong>Systemic infections</strong></td>
</tr>
<tr>
<td>bronchopneumonia</td>
<td>bacterial sepsis</td>
</tr>
<tr>
<td>pyelonephritis</td>
<td>bacterial</td>
</tr>
<tr>
<td>cholangiitis</td>
<td>endocarditis</td>
</tr>
<tr>
<td>purulent meningitis</td>
<td>leptospirosis</td>
</tr>
<tr>
<td>tonsillitis</td>
<td>relapsing fever</td>
</tr>
<tr>
<td>diphteria</td>
<td>amebic abscess</td>
</tr>
<tr>
<td>mesototisit</td>
<td></td>
</tr>
<tr>
<td>bacillary dysentery</td>
<td></td>
</tr>
<tr>
<td>pyogenic abscesses: liver,</td>
<td></td>
</tr>
<tr>
<td>subphrenical, retroperitoneal, ...</td>
<td></td>
</tr>
<tr>
<td>appendicitis</td>
<td></td>
</tr>
<tr>
<td>pyodermy, erysipelas</td>
<td></td>
</tr>
<tr>
<td>pyogenic arthritis</td>
<td></td>
</tr>
<tr>
<td>lymphadenopathy (plague,</td>
<td></td>
</tr>
<tr>
<td>tularemia, ..)</td>
<td></td>
</tr>
</tbody>
</table>

**EOSINOPHILIA:**
- filariasis
- schistosomiasis
- toxocarosis
- trichinellosis
- cysticercosis
- hydatidosis

DIFFERENCIAL DIAGNOSIS INCLUDES ALL AUTOCHTHONOUS DISEASES
## Acute Fever with Localizing Signs on Examination and with Neutrophil Leukocytosis

<table>
<thead>
<tr>
<th>Signs and symptoms</th>
<th>Disease</th>
<th>Investigations</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dyspnoe, cough, pleuritic pain, discoloured sputum</td>
<td>Bacterial pneumonia</td>
<td>Chest X-ray, sputum culture</td>
</tr>
<tr>
<td>Severe sore throat</td>
<td>Streptococcal tonsillitis, diphtheria</td>
<td>Through culture</td>
</tr>
<tr>
<td>Frequency, dysuria, loin pain</td>
<td>Pyelonephritis, UTI</td>
<td>US, urine culture</td>
</tr>
<tr>
<td>Headache, neck stiffness</td>
<td>Bacterial meningitis</td>
<td>LP, culture, latex agglut.</td>
</tr>
<tr>
<td>Ear secretion, headache</td>
<td>Otitis</td>
<td>Ear culture</td>
</tr>
<tr>
<td>Bloody diarrhea</td>
<td>Bacillary dysentery</td>
<td>Stool culture</td>
</tr>
<tr>
<td>Pain &amp; swelling at a joint</td>
<td>Septic arthritis</td>
<td>Joint aspiration, NMR</td>
</tr>
<tr>
<td>Bone pain (worse at night)</td>
<td>osteomyelitis</td>
<td>X-ray, CT, NMR</td>
</tr>
<tr>
<td>Local lymphadenopathy</td>
<td>Plague, abscess, tularemia</td>
<td>Culture, serology</td>
</tr>
<tr>
<td>Cutaneous inflammation</td>
<td>erysipelas, cellulitis</td>
<td>Culture, ASLO</td>
</tr>
</tbody>
</table>
# PARTICULAR FEVER CAUSES IN TROPICS

<table>
<thead>
<tr>
<th>SYMPTOMS AND SIGNS</th>
<th>DISEASE - INFECTION</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chronic cough for $&gt;$ 4 weeks or blood in sputum</td>
<td>Tuberculosis</td>
</tr>
<tr>
<td>Woman who has given birth in the last 4 weeks</td>
<td>Puerperal sepsis</td>
</tr>
<tr>
<td>A patient who underwent recently abdominal or pelvic surgery or abdominal or gynaecological disease</td>
<td>Liver, subphrenic, pelvic abscess</td>
</tr>
</tbody>
</table>
DIFFERENTIAL DIAGNOSIS OF CHRONIC FEVER
DURATION > 14 DAYS

➢ TO EXCLUDE TUBERCULOSIS AND HIV

• NEUTROPHIL LEUKOCYTOSIS PRESENT:
  – Abscesses (retroperitoneal, subfrenic); deep sepsis
  – Amebic liver abscess, extraintestinal amebiasis
  – Cholangiitis, bacterial liver abscess
  – Relapsing fever
  – Erythema nodosum leprosum

• LEUKOPENIA PRESENT:
  – Malaria
  – Visceral leishmaniasis
  – Disseminated tuberculosis
  – Brucellosis

• EOSINOPHILY PRESENT:
  – Schistosomiasis
  – Filariases
  – Trichinellosis, toxocarosis and other tissue helminthiases
DIFFERENTIAL DIAGNOSIS OF CHRONIC FEVER II

- NORMAL WBC COUNT:
  - Localized tuberculosis
  - Brucellosis
  - Secondary syphilis
  - Trypanosomiasis
  - Toxoplasmosis
  - Subacute bacterial endocarditis
  - Systemic lupus erythematosus

- VARIABLE WBC COUNT:
  - Tumours (lymphomas, Grawitz – renal cancer, colon cancer)
  - Connective tissue diseases
  - Drug reactions