

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, flies, lice biting
 - Spider, scorpion, snail, dog, cat, monkey biting
 - Contact with animals: dogs, cats, parrots, rodents, animal skin
- **PROPHYLAXIS:** Travel vaccination, antimalarials, repellents, mosquito nets, insecticides, sun lotions
- **DRUGS:** antibiotics, antimalarials, analgetics, infusions, blood transfusions
- **DIETE:** water, fruits, etc.
- **SEXUAL CONTACTS**
- **ALLERGY:** season, antibiotics, food, pollen, animals
- **MEDICAL PROBLEMS:** nausea, vomiting, diarrhea, fever
- **PROFESSION**
- **FAMILY HISTORY:** sickle cell disease, tuberculosis

CLINICAL AND LABORATORY EXAMINATION IN PATIENTS WITH FEVER AFTER RETURNING FROM TROPICS

MEDICAL EXAMINATION
MEDICAL HISTORY

**OTHER LABORATORY
& IMAGING EXAM.**

BASIC LABORATORY EXAM.:

- Thick and thin blood film
- Blood culture
- Blood count & differential count
- FW, CRP, Quick, PCT

SPECIAL LAB. EXAM
IDENTIFICATION OF
ETIOLOG. AGENTS

SEROLOGY
CULTURE Ag
DETECTION
MOLEC.METHODS



PHYSICAL EXAMINATION

- **SKIN**
 - exanthema, hemorrhagia, 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
- Mellioidosis - 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

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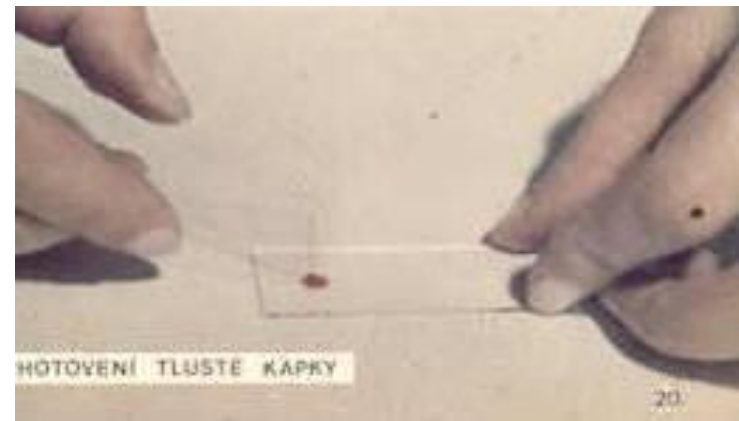
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FEVER DIAGNOSTICS

Thick and thin blood smears



Unstained thick and thin blood smears

FEVER DIAGNOSTICS



Thick and thin blood smears (Giemsa-Romanowski staining)

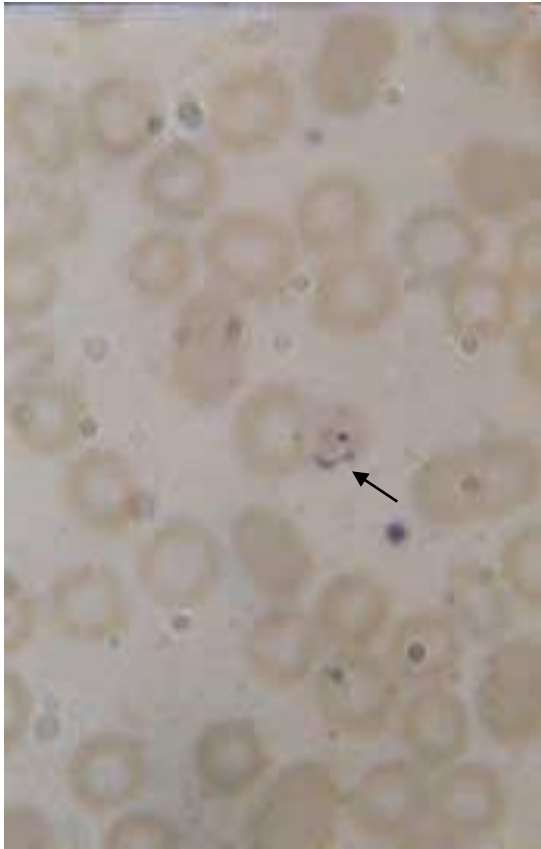
MALARIA DIAGNOSTICS – BLOOD SMEARS

- Smears, both thick and thin blood films, are made from peripheral 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: $50/\mu\text{l} \sim 0,001\%$ 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 **immediatelly**
 - smears are **repeated** every 12-24 h and **parasitaemia** is calculated to check the effect of antimalarials

MALARIA – DIAGNOSTICS III



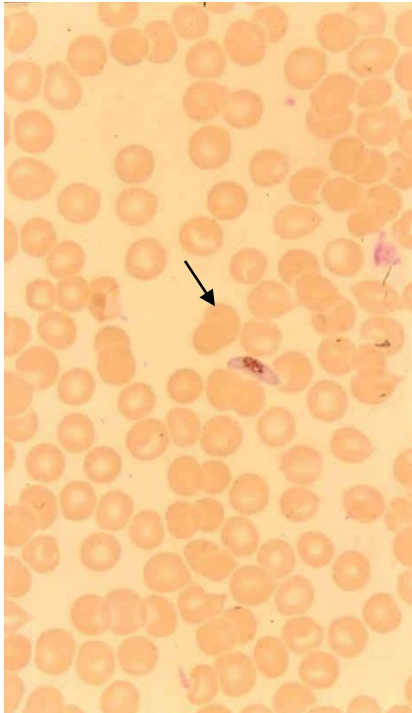
Plasmodium falciparum
– thin blood smear



Plasmodium falciparum
– thick blood smear

BLOOD SMEARS - INTRACELULAR

MALARIA



P. falciparum
gametocyte

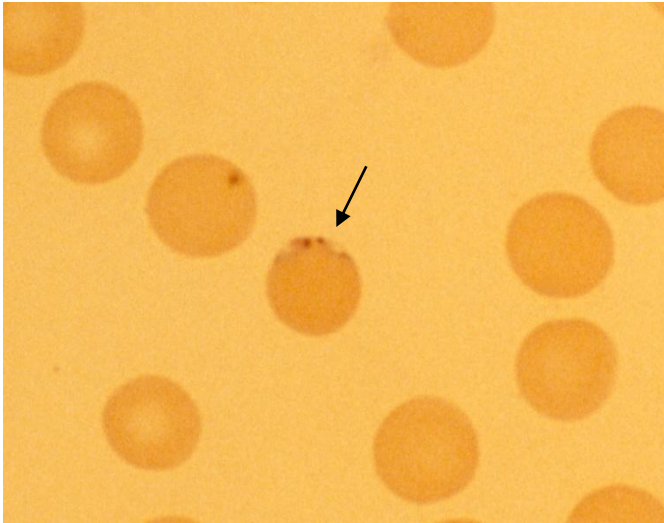


Plasmodium vivax - trophozoites

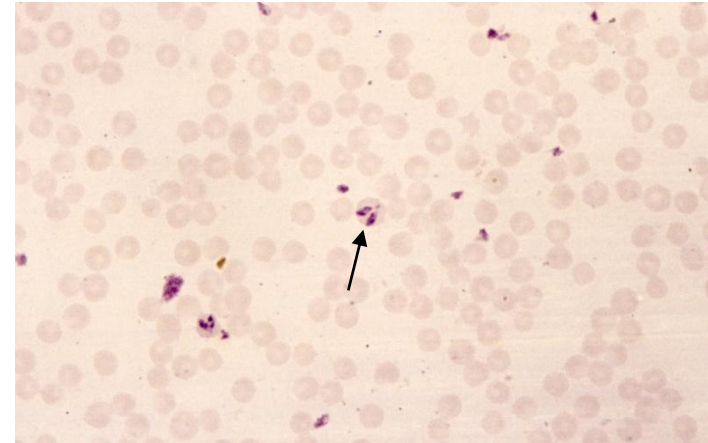


BLOOD SMEARS - INTRACELULAR

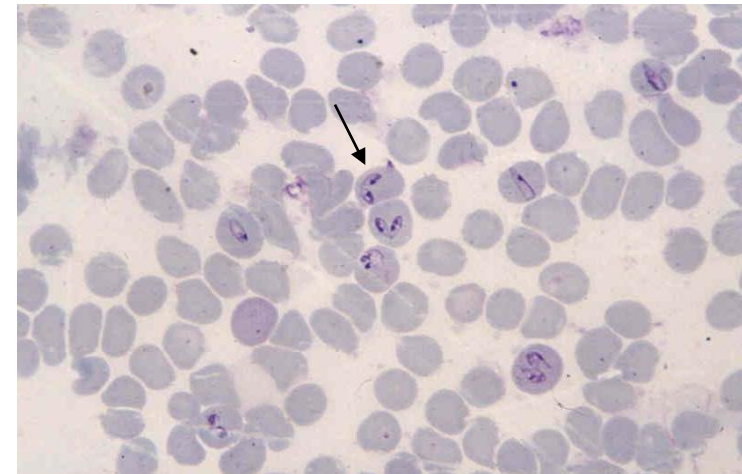
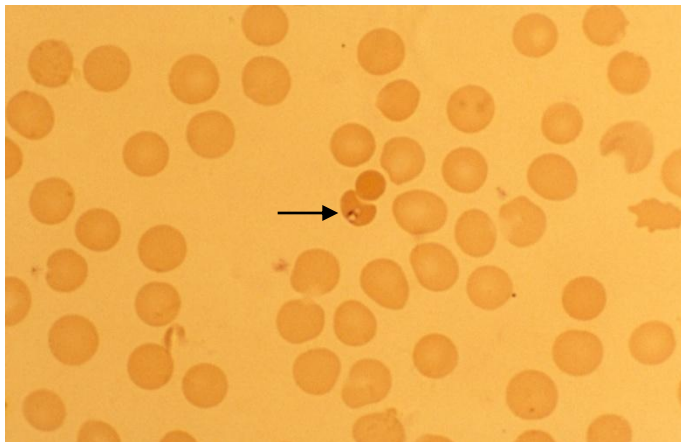
BABESIOSIS



Babesia microti



Babesia bigemina

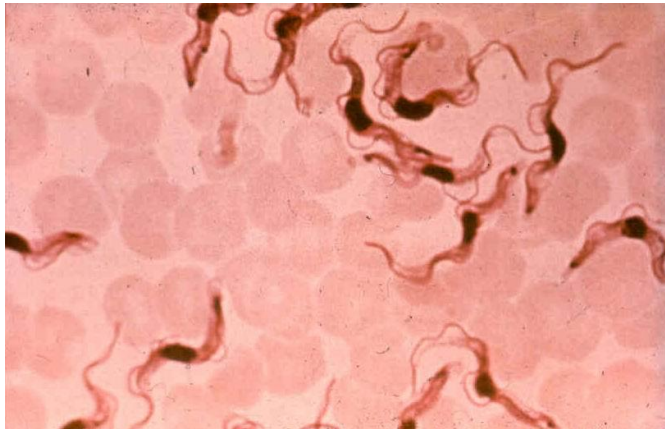


Babesia canis

BLOOD SMEARS - EXTRACELULAR

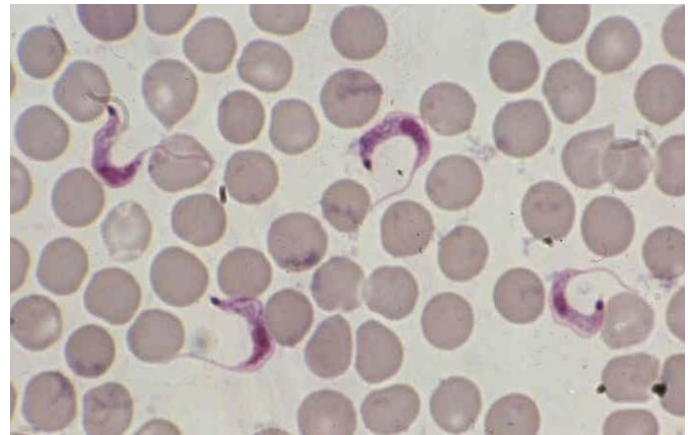
TRYPANOSOMIASIS

AFRICAN



Trypanosoma brucei

AMERICAN

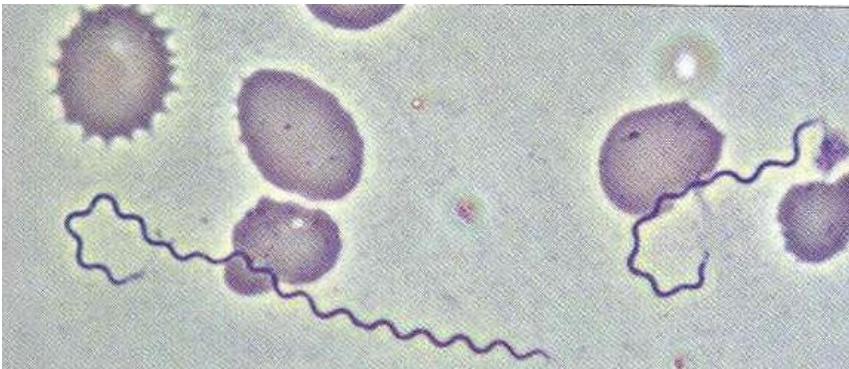


Trypanosoma cruzi

BLOOD SMEARS - EXTRACELULAR

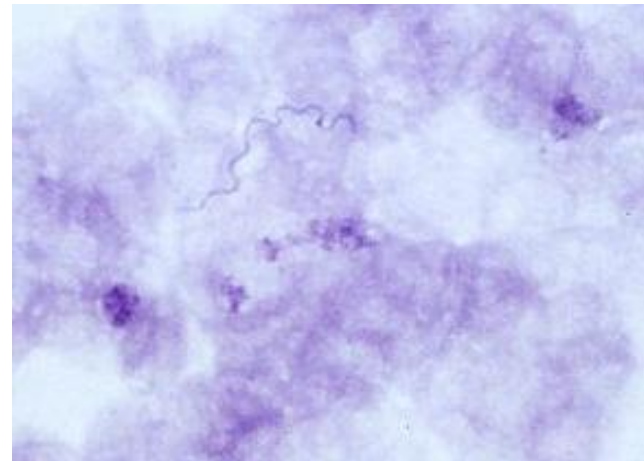
RELAPSING FEVER

EPIDEMIC



Borrelia recurrentis

ENDEMIC



Borrelia sp.

BLOOD SMEARS - EXTRACELULAR

FILARIOSIS



Loa loa



Wuchereria bancrofti

BLOOD SMEARS

POSITIVE:

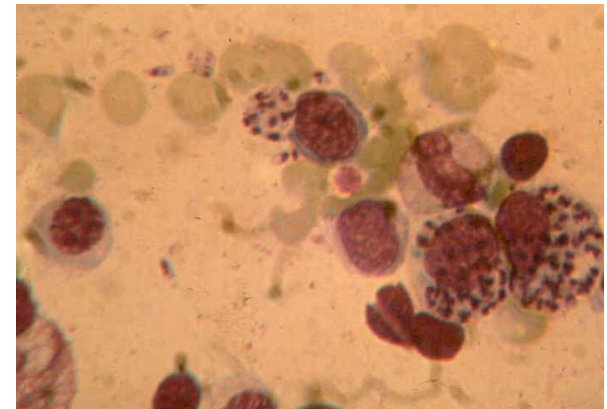
- Malaria
- Babesiosis
- Trypanosomiasis
- Filariasis
- Relapsing fever
- Bartonellosis
- Anaplasmosis, ehrlichiosis

NEGATIVE:

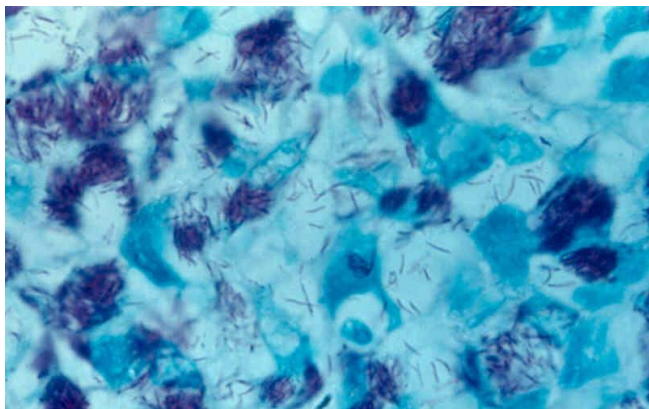
- Leishmaniasis
 - Buffy coat in HIV+
- Toxoplasmosis
- Amebiasis
- Schistosomiasis

POSITIVE BONE MARROW SMEARS PERIPHERAL BLOOD NEGATIVE

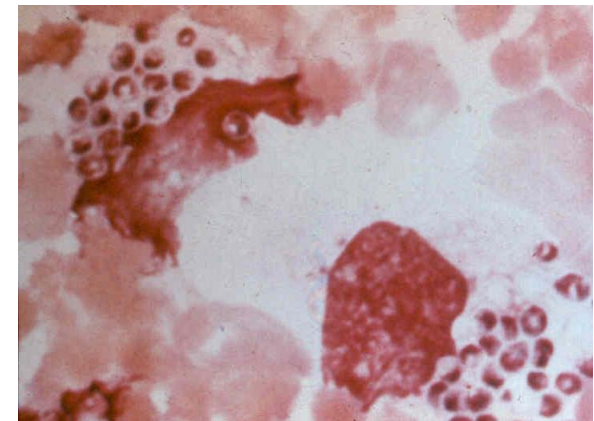
- Visceral leishmaniasis
- Histoplasmosis
- Lepromatous leprosy



Leishmania infantum



Mycobacterium leprae in the skin



Histoplasma capsulatum

LABORATORY INVESTIGATIONS IN FEVER DISEASES

FIRST LINE INVESTIGATIONS:

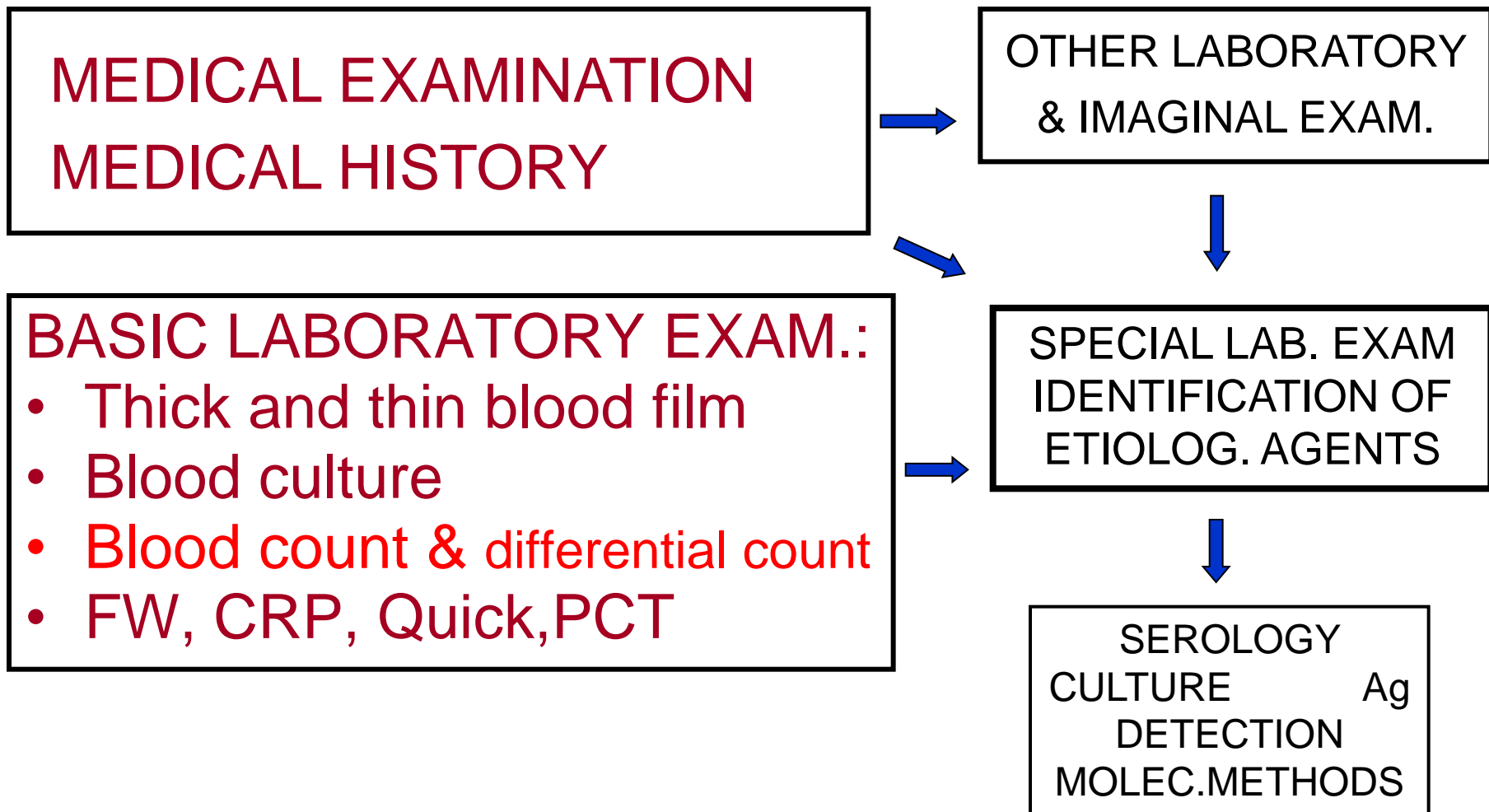
- Thin and thick blood smears
- **Blood cultures** (for aerobic and anaerobic bacteria)
- Total and differential white cell counts (WCC)
FW, CRP, PCT

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



DIFFERENTIAL DIAGNOSIS OF ACUTE FEVER

POLYMORPHONUCLEARS INCREASED		PMF NOT INCREASED
Focal symptoms	Systemic infections	
bronchopneumonia pyelonephritis cholangiitis purulent meningitis tonsillitis diphtheria mesootitis bacillary dysentery pyogenic abscesses: liver, subphrenical, retroperitoneal, ... appendicitis pyodermy, erysipelas pyogenic arthritis lymphadenopathy (plague, tularemia, ..)	bacterial sepsis bacterial endocarditis leptospirosis relapsing fever amebic abscess EOSINOPHILIA: filariasis schistosomiasis toxocarosis trichinellosis cysticercosis hydatidosis	<i>Viral infections:</i> <ul style="list-style-type: none"> ▪ measles and other exanthematic infections ▪ viral hepatitis ▪ dengue fever, haemorrhagic fevers ▪ HIV - acute infection <i>Bacterial infections:</i> <ul style="list-style-type: none"> ▪ rickettsiosis ▪ typhoid fever <i>Protozoal infections:</i> <ul style="list-style-type: none"> ▪ malaria ▪ trypanosomiasis ▪ visceral leishmaniasis ▪ toxoplasmosis

DIFFERENTIAL DIAGNOSIS INCLUDES ALL **AUTOCHTONOUS DISEASES**

ACUTE FEVER WITH LOCALIZING SIGNS ON EXAMINATION AND WITH NEUTROPHIL LEUKOCYTOSIS

Signs and symptoms	Disease	Investigations
Dyspnoea, cough, pleuritic pain, discoloured sputum	Bacterial pneumonia	Chest X-ray, sputum culture
Severe sore throat	Streptococcal tonsillitis, diphtheria	Throat culture
Frequency, dysuria, loin pain	Pyelonephritis, UTI	US, urine culture
Headache, neck stiffness	Bacterial meningitis	LP, culture, latex agglut.
Ear secretion, headache	Otitis	Ear culture
Bloody diarrhea	Bacillary dysentery	Stool culture
Pain & swelling at a joint	Septic arthritis	Joint aspiration, NMR
Bone pain (worse at night)	osteomyelitis	X-ray, CT, NMR
Local lymphadenopathy general. lymphadenopathy	Plague, abscess, tularemia	Culture, serology
Cutaneous inflammation	erysipelas, cellulitis	Culture, ASLO

PARTICULAR FEVER CAUSES IN TROPICS

SYMPTOMS AND SIGNS	DISEASE - INFECTION
Chronic cough for > 4 weeks or blood in sputum	Tuberculosis
Woman who has given birth in the last 4 weeks	Puerperal sepsis
A patient who underwent recently abdominal or pelvic surgery or abdominal or gynaecological disease	Liver, subphrenic, pelvic abscess

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