
The Returning Traveler

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- Screening of returned travelers can represent significant portion of the time of travel medicine centers
- Screening is undertaken to detect specific conditions and/or risks factors that have health implication
  - Assess risk
    - Long term or short term travel
    - Category of Traveler
    - Activities (water contact, vaccination, malaria prophylaxis)
    - Specific Risks (STDs, Food borne illness, vector illness)
  - Physical Exam
  - Diagnostic testing

Screening Tests

- STDs
  - Hepatitis B 11/100 person years in missionaries
  - Peace corps workers only a 32% use of condoms
  - HIV, Chlamydia, HepB, gonorrhea, syphilis

- Parasitic Diseases
  - Overall 4 to 10% depending on length of travel
  - Stool O&P
  - Specific serology (i.e. Schistosomiasis for water exposure)
  - Blood smears and filarial serology not useful in asymptomatic patients

- Routine CBC
  - Eosinophilia (>450 cells/mm^3)
  - Positive predictive value only 14%.

Fever in the Returning Traveler

- Fever in a traveler must be evaluated promptly as a delay in diagnosis and treatment can have significant consequences (i.e. the development of cerebral malaria or the spread of contagious diseases)

- A key question is: "Where have you been and what did you do during your travel?"

- Remember that just because someone has traveled it doesn't mean that they have an exotic disease!

Causes of Fever after Travel

Diagnosis	MacLean (n=587)	Doherty (n=195)
Malaria	32 %	42 %
Undiagnosed	25	25
Other tropical		
Diarrheal illness	4.5	6
Dengue	2	6
Enteric Fever	2	2
Rickettsia	1	0.5
Amebic liver abscess	0.5	0
Cosmopolitan		
Hepatitis	6	5
Respiratory	11	2.5
Urinary (UTI)	4	2.5
EBV (mono)	2	0.5
TB	1	2
Pharyngitis	1	1
Meningitis	1	1
Acute HIV	0.3	1
Miscellaneous	6.3	5

No prophylaxis = malaria

Chemo.	USA	UK	Canada
none	84.2%	81%	97%
MFQ	5.8%	4%	3%

MMWR 2001;50:S1-44. Kain et al CID 1998;27:142. Eurosurveillance 1998;3:40

Who dies from Traveler's Malaria?

	USA & Canada (n=21)	Total
no chemo.	21	100%
Delay seeking care	1	5%
Missed by MD	13	62%
Lab misDx	9	43%
misRx	11	52%

MMWR July 20, 2001 & 1999;48:SS-1.
Kain et al. CMAJ 2001;164:654

Common Causes of Fever After Tropical Travel

- Malaria
- Respiratory tract infections (including pneumonia)
- Diarrhea illness
- Hepatitis
- Urinary tract infection
- Dengue fever
- Enteric fever
- Rickettsial infection
- Infectious mononucleosis
- Pharyngitis

Disease	*Distribution*	*Vector*	*Incubation period*
Malaria—*Plasmodium vivax, Plasmodium falciparum, Plasmodium ovale*	Worldwide	Mosquito, blood transfusion, IVDA	8–15 d
Malaria—*Plasmodium malariae*	Worldwide	Mosquito, blood transfusion, IVDA	15–30 d
African trypanosomiasis	Sub-Saharan Africa	Tsetse fly	10–21 d after chancre appears
Schistosomiasis	Africa, South and Southeast Asia, China	Freshwater exposure	4–8 wk
Leishmaniasis	South and Southeast Asia, Africa, Middle East, Central and South America	Sandflies	(Visceral disease) 3–10 mo
Dengue	Worldwide	*Aedes* mosquitoes	4–7 d
Yellow fever	15 degrees North or South of the equator	*Aedes* mosquitoes	3–8 d; remits for 1–2 d and then severe illness
Primary HIV disease	Worldwide	Sexual contact, IVDA, transfusions	3–21 d
Hepatitis A	Worldwide	Fecal-Oral	15–45 d
Rabies	Worldwide	Animal bite	30–120 d
Arboviral fevers	Variable	Mosquitoes, ticks	3–6 d for some, 7–10 d for others
Lassa fever	West-Central Africa	Rodent	7–14 d
Ebola/Marburg	Africa	Human contact	7–21 d
African tick bite fever	Sub-Saharan Africa, South Africa	Tick	4–7 d
Mediterranean spotted fever	Sub-Saharan Africa	Tick	4–7 d
Scrub typhus	Southeast Asia, South Asia, Africa	Mites, chiggers	8–12 d
Epidemic typhus	Southeast Asia, South Asia, Africa, South and Central America	Lice	8–12 d
Murine typhus	Worldwide	Fleas	8–14 d
Q fever	Worldwide	Parturient ungulates; ticks	10–14 d
Leptospirosis	Worldwide	Freshwater exposure; mammals (urine, tissue)	Primary phase: 10–21 d; remits for 2–3 d; secondary phase: up to 4 wk
Bubonic plague	Worldwide	Rat flea	3–5 d
Brucellosis	Worldwide	Unpasteurized dairy products, undercooked meat	2–3 wk
Tuberculosis	Worldwide	Respiratory	Months

* HIV indicates human immunodeficiency virus; IVDA, intravenous drug abuse.

Incubation less than 14 days Undifferentiated fever

- Malaria
- Dengue
- Spotted Fever rickettsiae
- Typhus group rickettsiae
- Scrub Typhus
- Leptospirosis
- Typhoid and paratyphoid fevers
- Campylobacteriosis, salmonellosis, shigellosis
- Brucellosis
- Acute HIV
- Tularemia
- Relapsing Fever
- Toxoplasmosis
- Erhlichiosis
- African Trypanosomiasis (T. brucei rhodesiense)
- American Trypanosomiasis

Incubation 2-6 weeks

- Malaria
- Typhoid and Paratyphoid fevers
- Hepatitis A and E
- Acute Schistosomiasis (Katayama syndrome)
- Leptospirosis
- Amebic Liver abscess
- Q fever
- HIV, acuter
- African tryps
- Viral hemmorrhagic fever (hantaviruses longer incubation)
- Brucellosis
- Tuberculosis
- Cytomegalovirus (acute)
- Toxoplasmosis

Incubation > 6 weeks

- Malaria
- Tuberculosis
- Hepatitis B
- Leishmaniasis, visceral
- Schistosomiasis
- Amebic liver abscess
- Filariasis, lymphatic
- Hepatitis E
- Rabies
- African trypansosomiasis (T.b. gambiense)
- Fungal infections, including histoplasmosis, coccidioidomycosis, paracoccidioidomycosis, others
- Brucellosis
- Meloidosis

Activity based risk factors

Ingestion:
- Consumption of untreated water—hepatitis A and E, amoebiasis, cholera
- Consumption of unpasteurized dairy products—brucellosis, *Salmonella*, Q fever
- Undercooked meat—cestodes, trichinosis, *Salmonella*, *Escherichia coli*

Animal contact:
- Animal (mammal) contact—rabies, Q fever, typhus, tularemia, brucellosis, leptospirosis, echinococcosis, anthrax
- Mosquitoes—dengue, malaria, yellow fever, arboviruses
- Tsetse flies—African trypanosomiasis
- Sand flies—filariasis, leishmaniasis
- Hard ticks—Mediterranean spotted fever, African tick typhus, North Asian tick typhus, Queensland tick typhus, arboviruses
- Fleas—murine typhus, plague
- Lice—epidemic (louseborne) typhus, relapsing fever
- Mites—scrub typhus

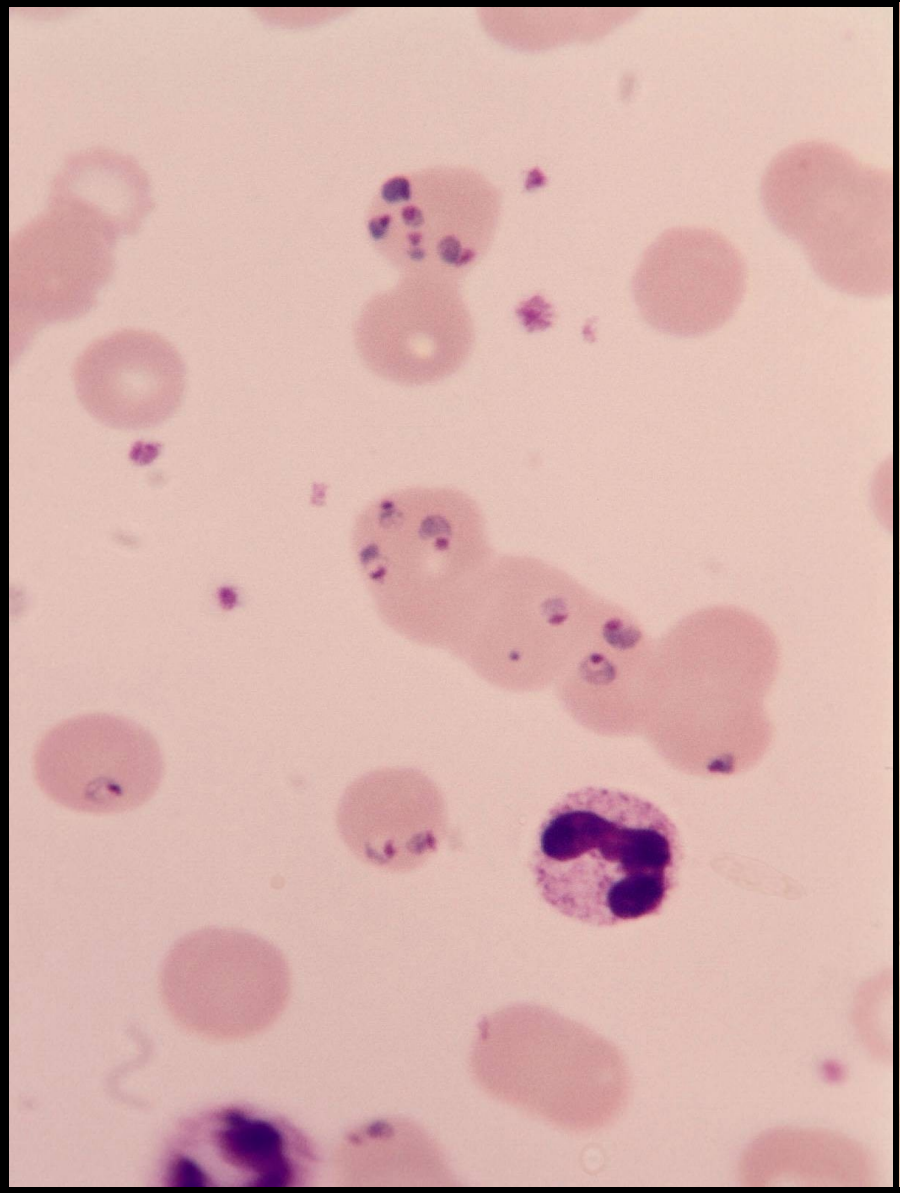
Recreation:
- Freshwater exposure—leptospirosis, schistosomiasis
- Barefoot exposure—strongyloides, cutaneous larval migrans
- Sexual contact—HIV, hepatitis B and C, syphilis, gonorrhea, herpes simplex
- Sick contacts—TB, meningitis, viral hemorrhagic fevers
- IVDA/Transfusions—HIV, hepatitis B and C, malaria, toxoplasmosis, babesiosis

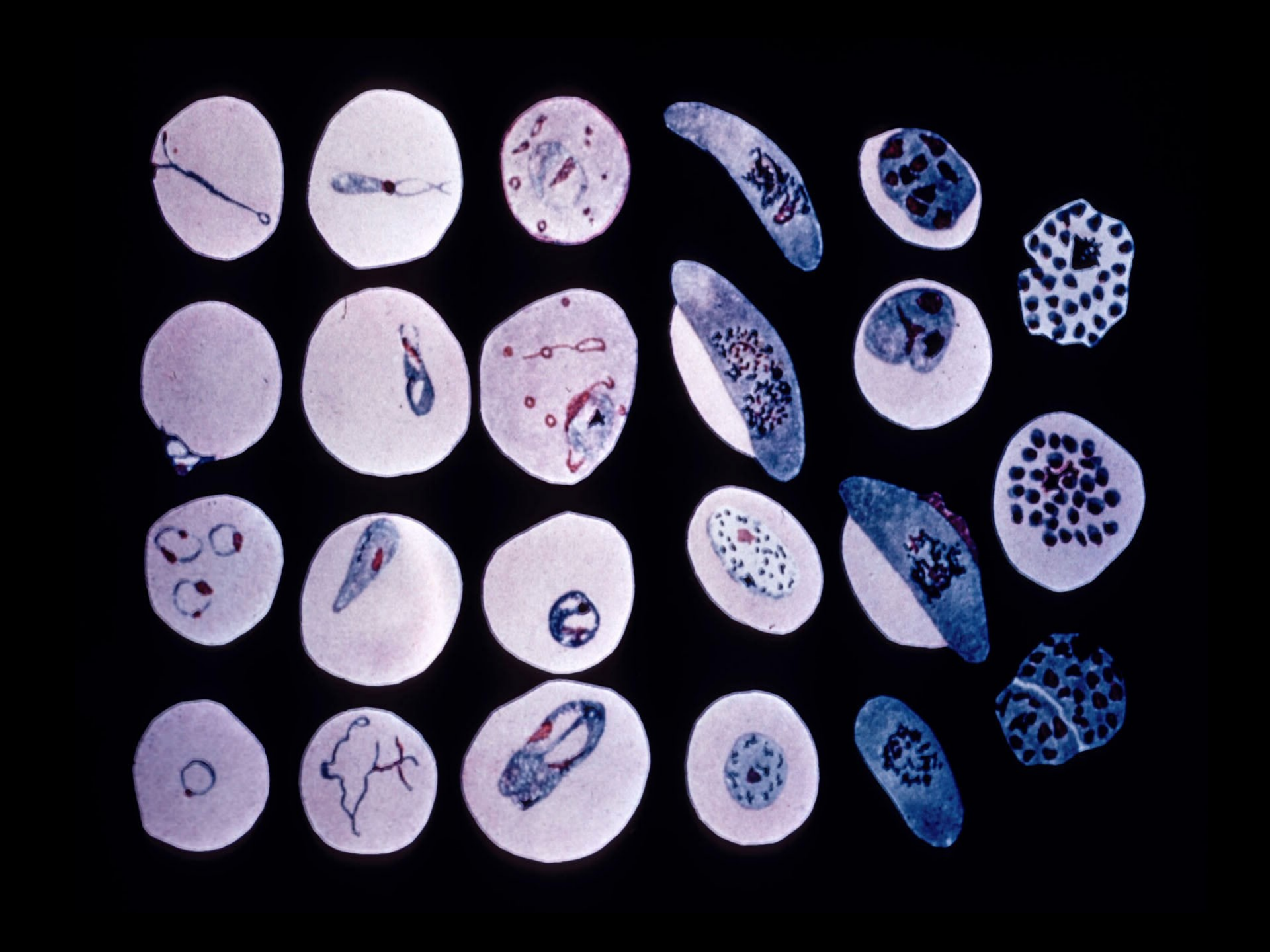
*HIV indicates human immunodeficiency virus; IVDA, intravenous drug abuse; and TB, tuberculosis.

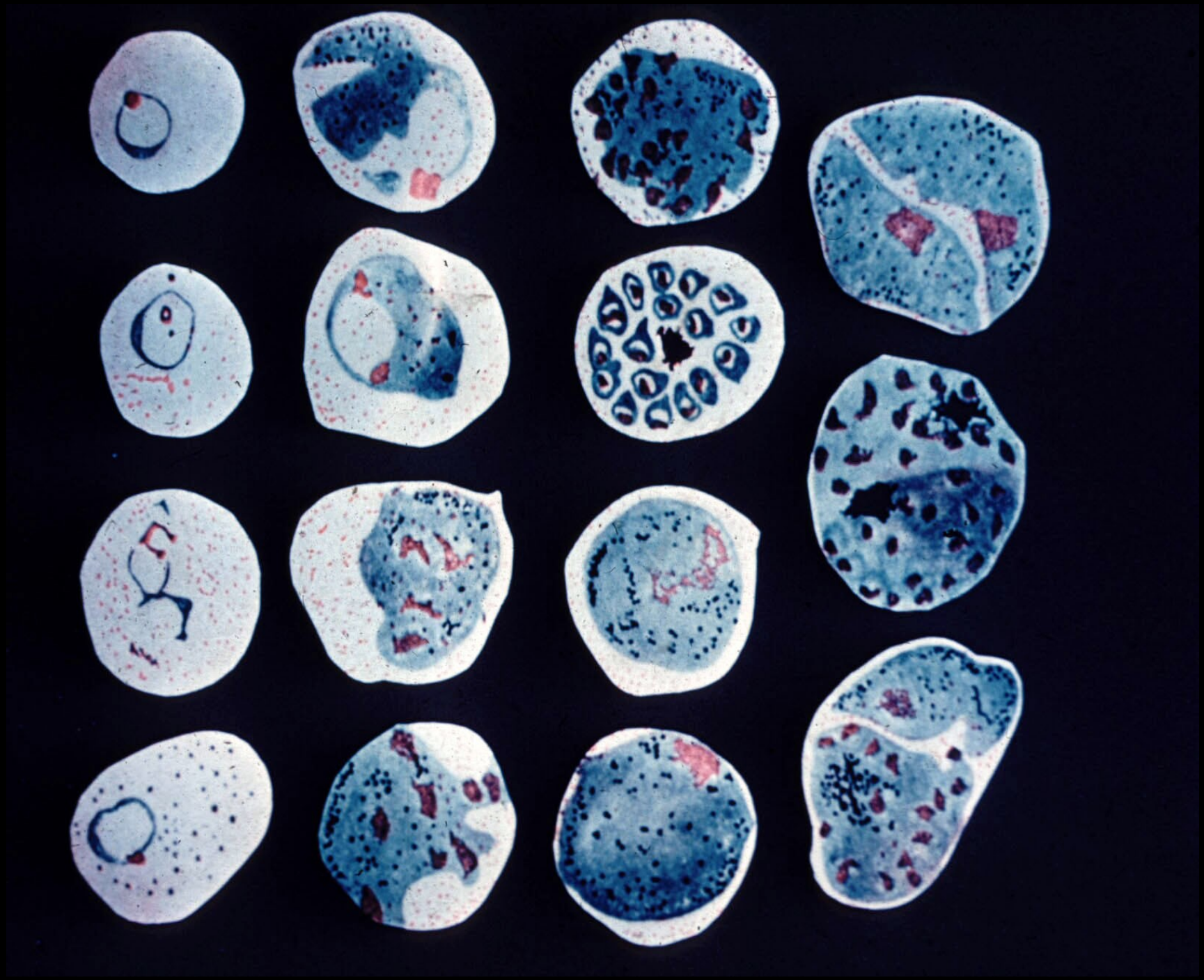
Basic Diagnostic Tests for a Traveler with Fever

Complete blood count with manual differential—the Wright-stained slide will be available within minutes for hematolymphatic parasite detection.
Thick and thin peripheral blood smears—staining and examination take about 1 h.
Serum electrolytes
Liver profile
Urinalysis
Blood culture
Stool for ova and parasites, culture and fecal leukocytes
Chest radiographs

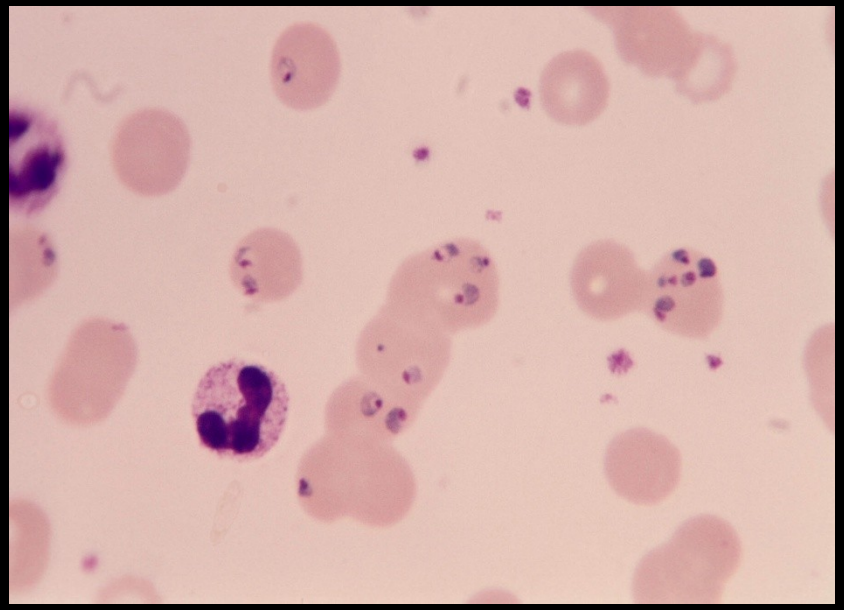
*If the patient has pharyngitis and lymphadenopathy—Monospot; if the patient has liver function test abnormalities and right upper quadrant tenderness—hepatitis panel; if the patient has anemia, thrombocytopenia, or any hemorrhagic manifestation-prothrombin time/activated partial time/fibrinogen or disseminated intravascular coagulation panel.



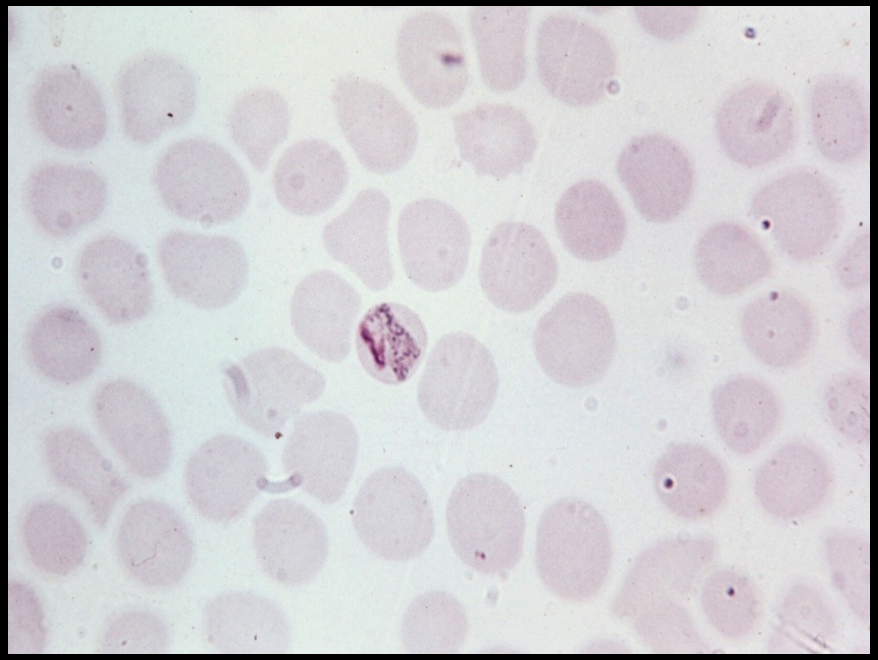




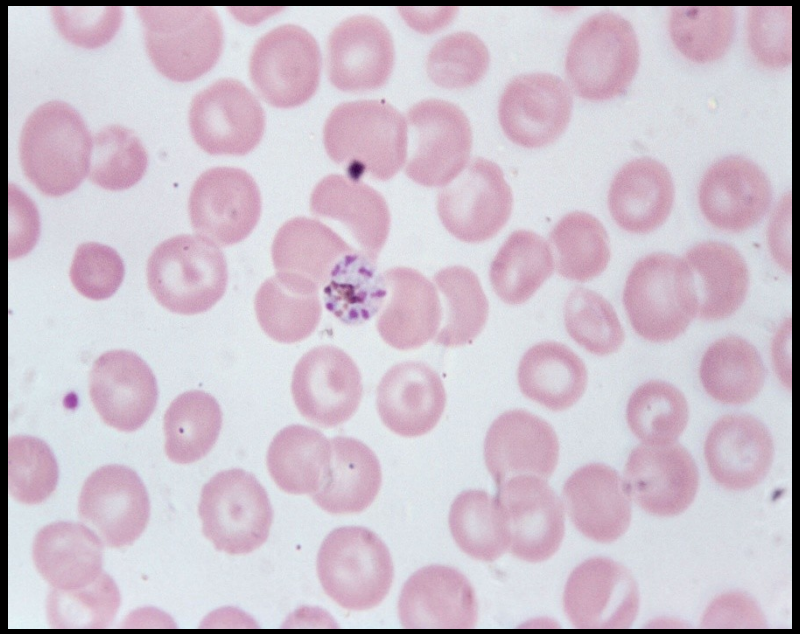
P. falciparum - gametocyte



P. falciparum – ring stages



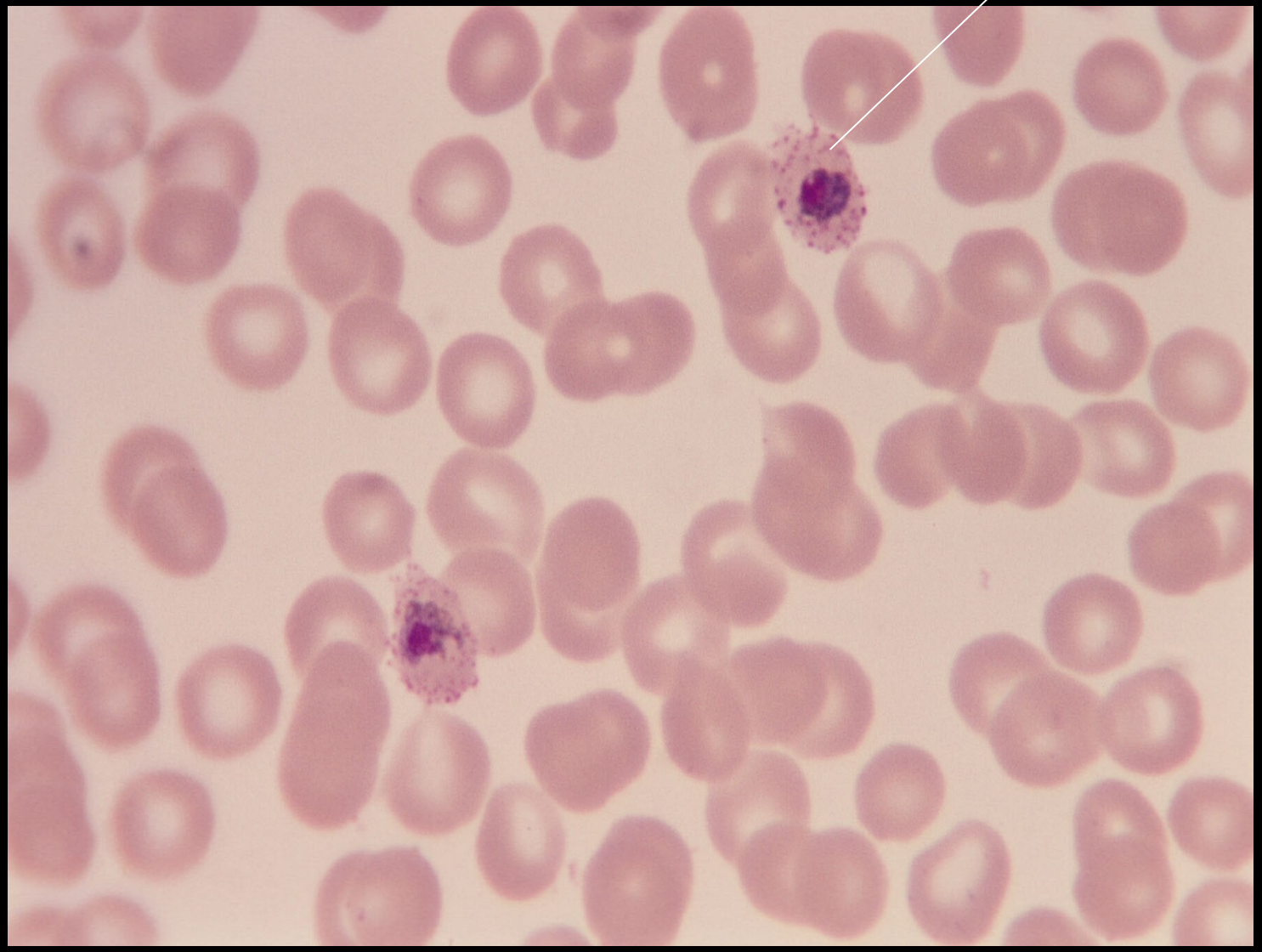
P. malariae - band stage (trophozoite)



P. malariae rosette (segmented merozoite stage)

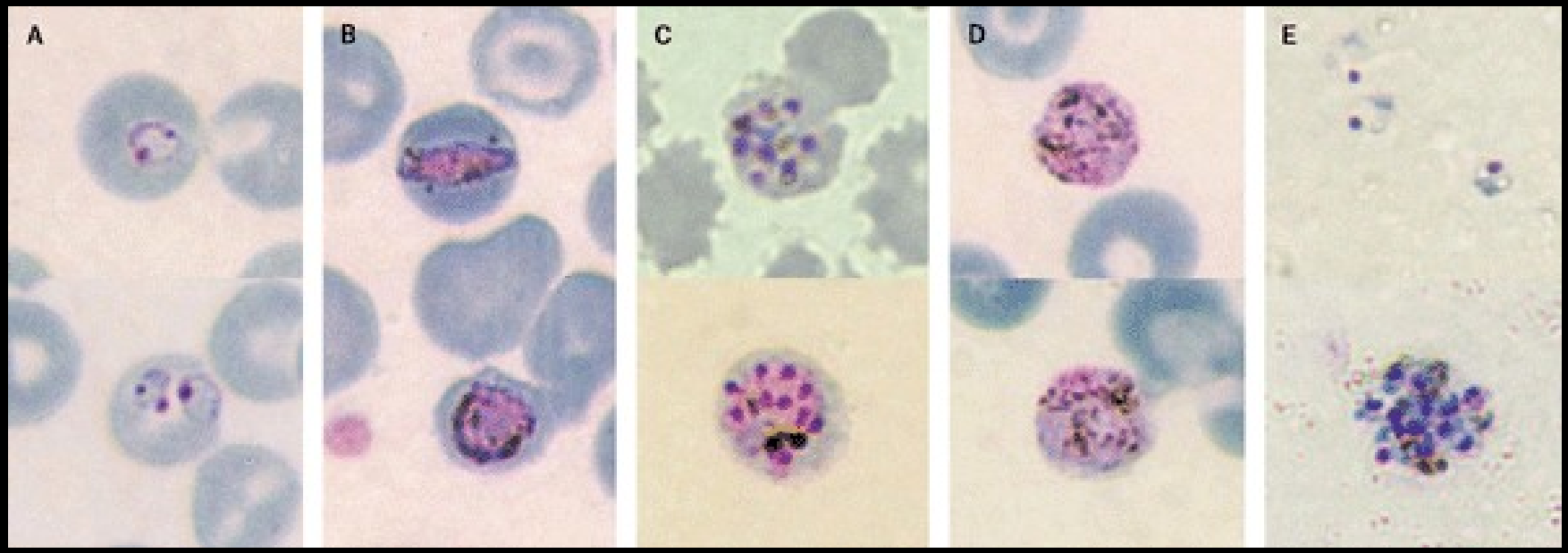
P. vivax

P. ovale - trophozoite stage

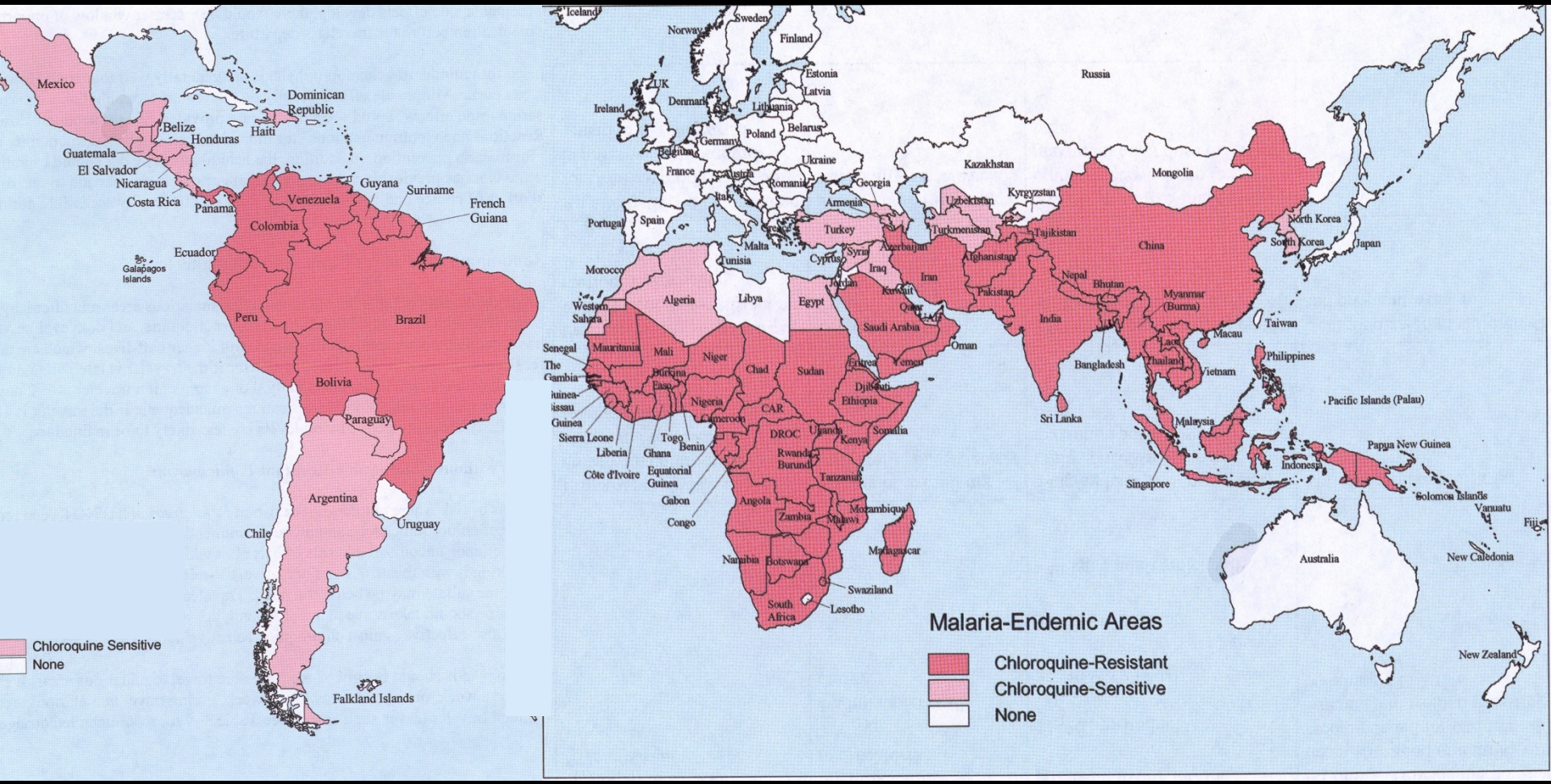


Plasmodium knowlesi

the fifth species of malaria in humans
a zoonotic malaria species



Malaria Endemic Areas



Treatment Strategies

- **Chloroquine (CQ) sensitive (all species)**
  - **CQ + primaquine (*P. vivax/ovale*)**
- **Chloroquine Resistance (or unknown)**
  - **quinine, mefloquine,** Atovaquone/proguanil **or artemesin**
- **Severe or Complicated Malaria**
  - **i.v. infusion of quinidine (or quinine)**
  - **i.v. artemisinin derivatives (if available)**

Treatment of Malaria
Chloroquine Sensitive

Chloroquine 600mg base then 500mg base at 12, 24 and 48 hr

- *P. malariae*
- *P. falciparum* (only in very limited geographic areas such as the Haiti and parts of Central America)
- *P. vivax* and *P. ovale* need in addition radical cure with Primaquine (30 mg base/d x14d)

Plasmodium vivax Resistance

- Chloroquine resistance is found in Indonesia and Oceania with increasing reports in South and Central America
  - Treatment
    - Quinine (650mg TID x 7days) plus Doxycycline (100 mg BID x 7days)
  - Alternative treatments
    - Mefloquine (750 mg followed in 12 hr by 500mg)
    - Chlorquine plus primaquine (30mg base/ day)

Plasmodium falciparum Chloroquine Resistance

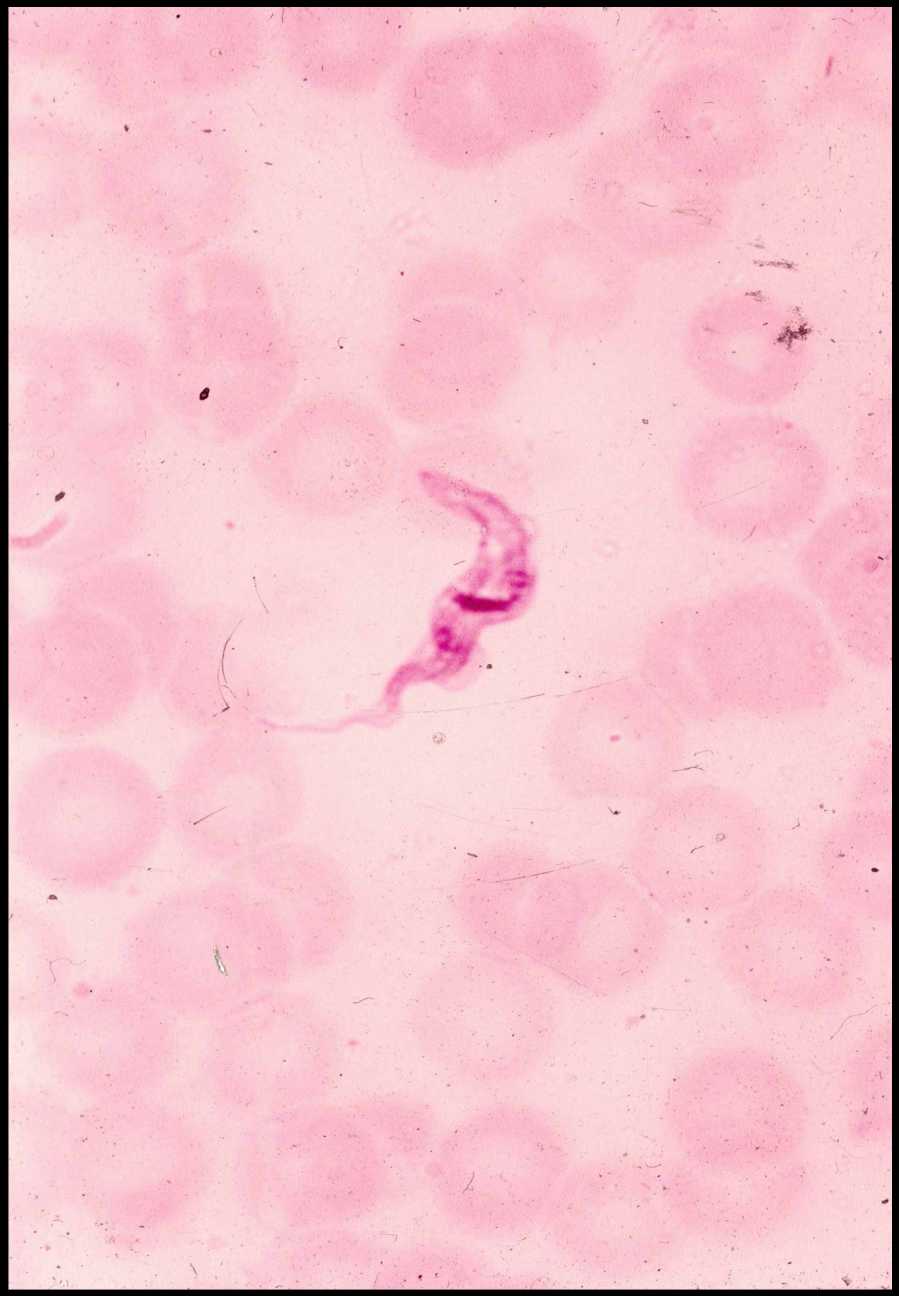
- Treatment
  - Quinine (650mg TID x 7days) plus
    - Doxycycline (100 mg BID x 7days) or
    - Clindamycin (20 mg/kg/d divided TID x 7days)
  - Atovaquone/proguanil (4 adult tablets/d x 4 days)
  - Quinidine (10mg/kg loading dose then 0.02mg/kg/min until PO therapy can be started)

- Alternative treatments
  - Mefloquine (750 mg followed in 12 hr by 500mg)
  - Atesunate (4mg/kg/d x 3 days) plus mefloquine

Specialized diagnostic testing is based on symptoms and risk

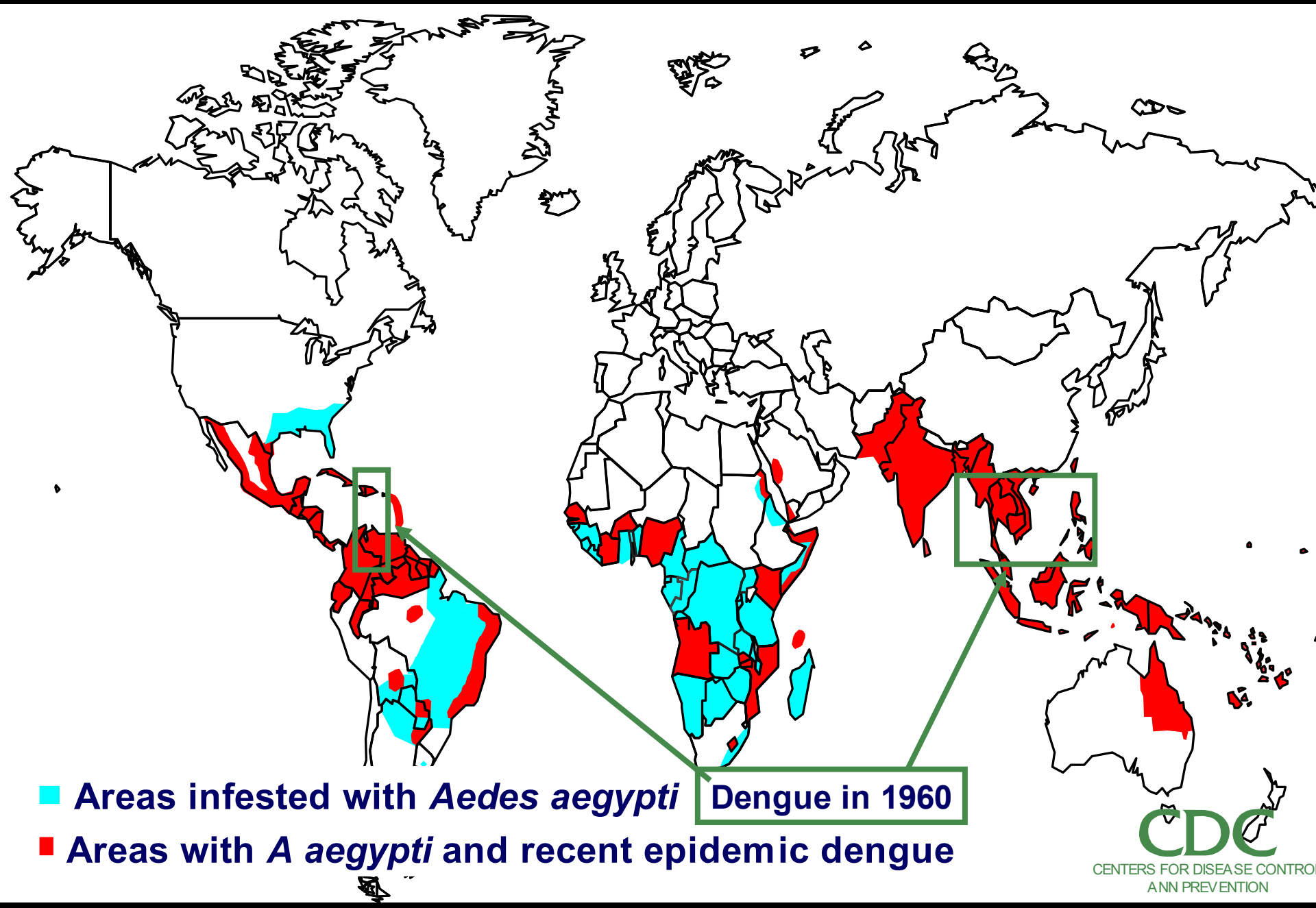
1) Lumbar puncture—in any instance of altered mental status or suspected meningoencephalitis (even arboviral) or to diagnose CNS involvement in leptospirosis or early trypanosomiasis.
   Cell count and differential
   Protein and glucose
   Bacterial culture and gram stain
   Viral culture
   (Centrifuged, giemsa or acridine orange–stained slide for trypanosomes or leptospires, if suspected; CSF total IgM to rule out occult CNS infection when the WBC is low)
2) RPR, hepatitis B and C panel, HIV—if an STD is possible by activity-based risk.
3) RUQ ultrasound or CT scan of the abdomen—when significant focal findings on abdominal exam or lab abnormalities raise the possibility of a structural lesion: ecchinococcal cyst, liver flukes, amoebic liver disease, or high-volume helminthic infestation with intestinal obstruction.
4) MRI of the brain and spinal cord—when acute, focal, or progressive,* neurological findings could be manifestations of cerebral or neuroschistosomiasis, CNS parasites (toxoplasmosis), or helminthic (neurocysticercosis) infestation.

*CNS indicates central nervous system; CSF, cerebrospinal fluid; CT, computed tomographic; HIV, human immunodeficiency virus; IgM, immunoglobulin M; MRI, magnetic resonance imaging; RPR, rapid plasma reagin; RUQ, right upper quadrant; STD, sexually transmitted disease; and WBC, white blood cell count.



Exotic Viral Diseases in Travelers

Disease	Family	Vector	Geography
Venezuelan equine encephalitis	Togavirus	*Haemagogus* mosquitoes	South America
Mayaro	Togavirus	*Haemagogus* mosquitoes	Amazon basin, northern South America
Chikungunya	Togavirus	*Aedes* mosquitoes	South Asia, Philippines
Yellow fever	Flavivirus	*Aedes aegypti*	15 degrees North and South latitude of equator
Dengue	Flavivirus	*A. aegypti* and *Aedes albopiclus*	Caribbean, Central and South America, South and Southeast Asia
Japanese B encephalitis	Flavivirus	*Culex* mosquitoes	Southeast Asia, South Asia, China, Australia (1995)
Murray Valley encephalitis	Flavivirus	*Culex* mosquitoes	Australia
West Nile virus	Flavivirus	Mosquito—*Culex* and *Anopheline* spp in Europe	Africa, Middle East, South France, and Eastern Europe, New York and other states (1999)
Central European tick-borne encephalitis	Flavivirus	*Dermacentor*, *Ixodes*, and *Haemaphysalis* spp	Eastern Europe, southern Europe, western Russia
Hantavirus	Bunyavirus	Rodent urine and feces	Manchuria, Korea, Japan, United States
Rift Valley hemorrhagic fever	Bunyavirus	Mosquito	Africa
Crimean-Congo hemorrhagic fever	Bunyavirus	*Dermacentor* and *Hyalomma* spp	Crimea, Africa, Europe, Asia
Lassa hemorrhagic fever	Arenavirus	Rodent	West Africa
Argentine (Junin) hemorrhagic fever	Arenavirus	Rodent	Argentina
Bolivian (Machupo) hemorrhagic fever	Arenavirus	Rodent	Northeast Bolivia
Marburg	Filovirus	Human contact	Sub-Saharan Africa
Ebola	Filovirus	Human contact	Africa


Areas infested with *Aedes aegypti*
Areas with *A aegypti* and recent epidemic dengue
Dengue in 1960
CDC
CENTERS FOR DISEASE CONTROL
ANN PREVENTION

Skin Diseases in the Returning Traveler

Systemic illness with skin disease

Petechial or Hemorrhagic

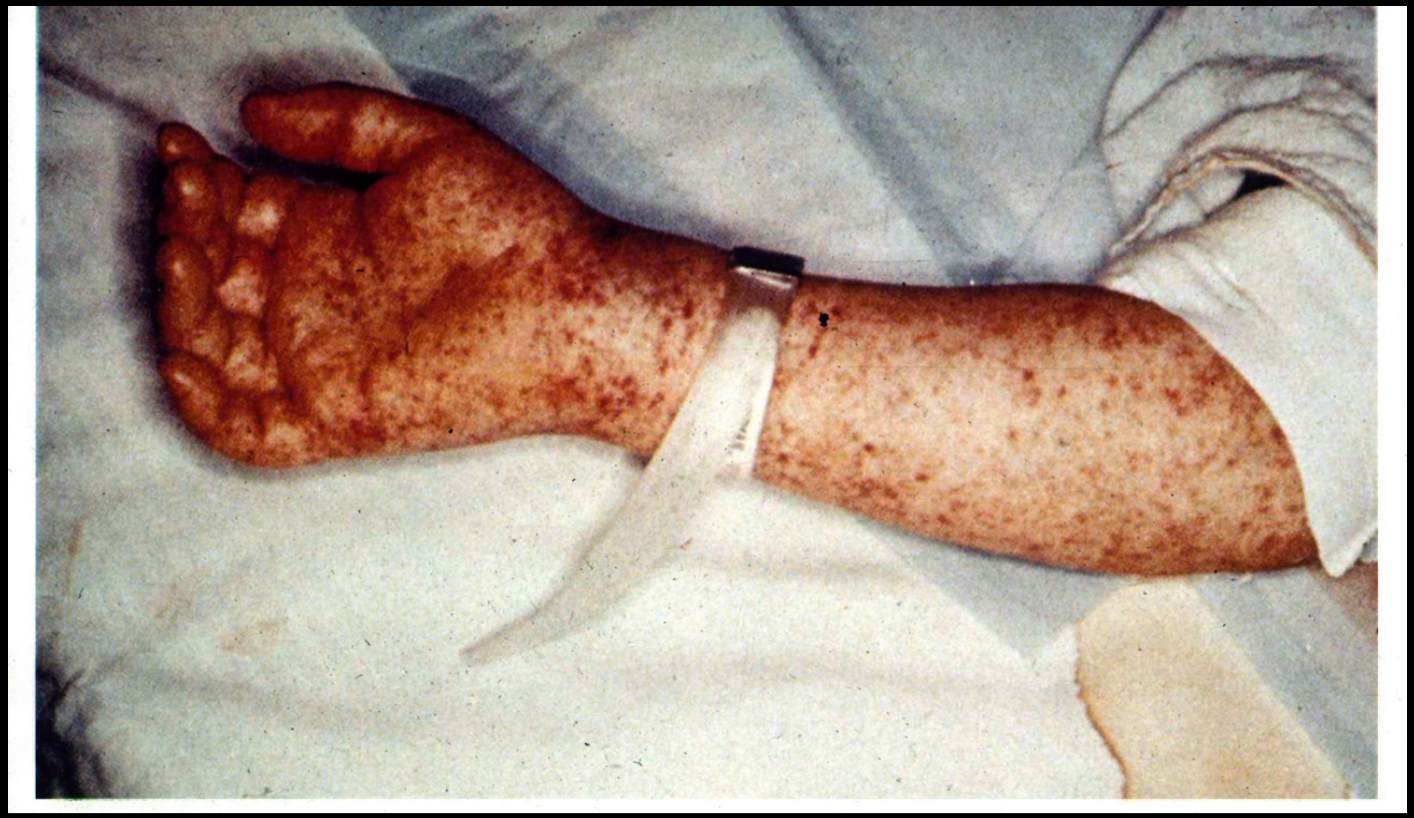
e.g... Rickettsia, Dengue, Leptospirosis, Hemorrhagic fevers (Lassa, Ebola etc)

Diffuse

e.g... Rat-bite fever, Measles, Brucellosis

Focal

e.g... Lyme, Trypnosomiasis, Syphilis



Pruritic Skin Lesions in the Returning Traveler

Helminthic infections

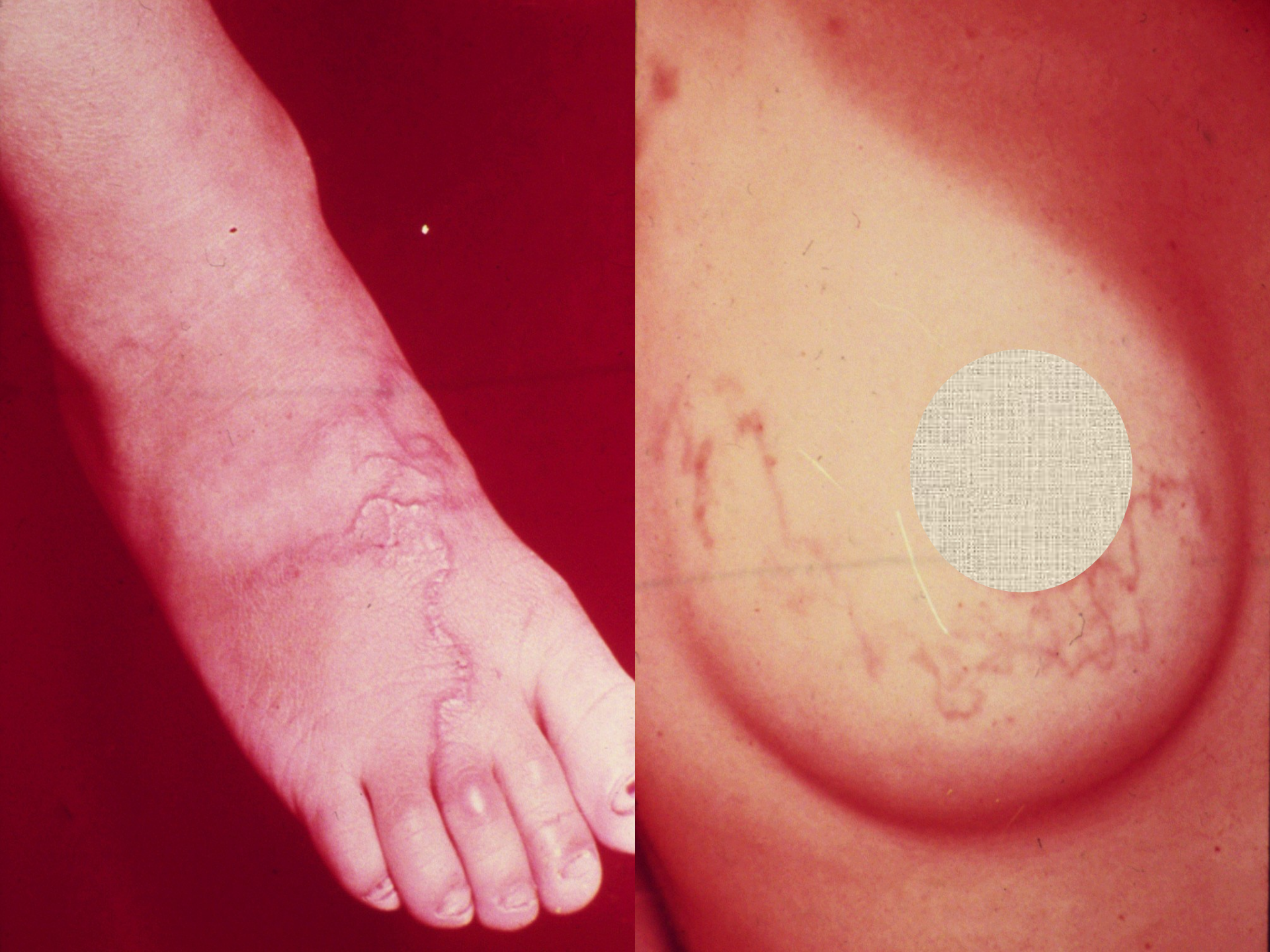
- Cercarial dermatitis (swimmers itch)
- Cutaneous larva migrans
- Dracunculiasis
- Hookworm
- Loiasis
- Onchocerciasis
- Pin worms
- Stronglyloidiasis
- Mansonelliasis

Arthropod Bites and infestations

- Chiggers
- Fleas
- Lice
- Mosquitoes
- Scabes

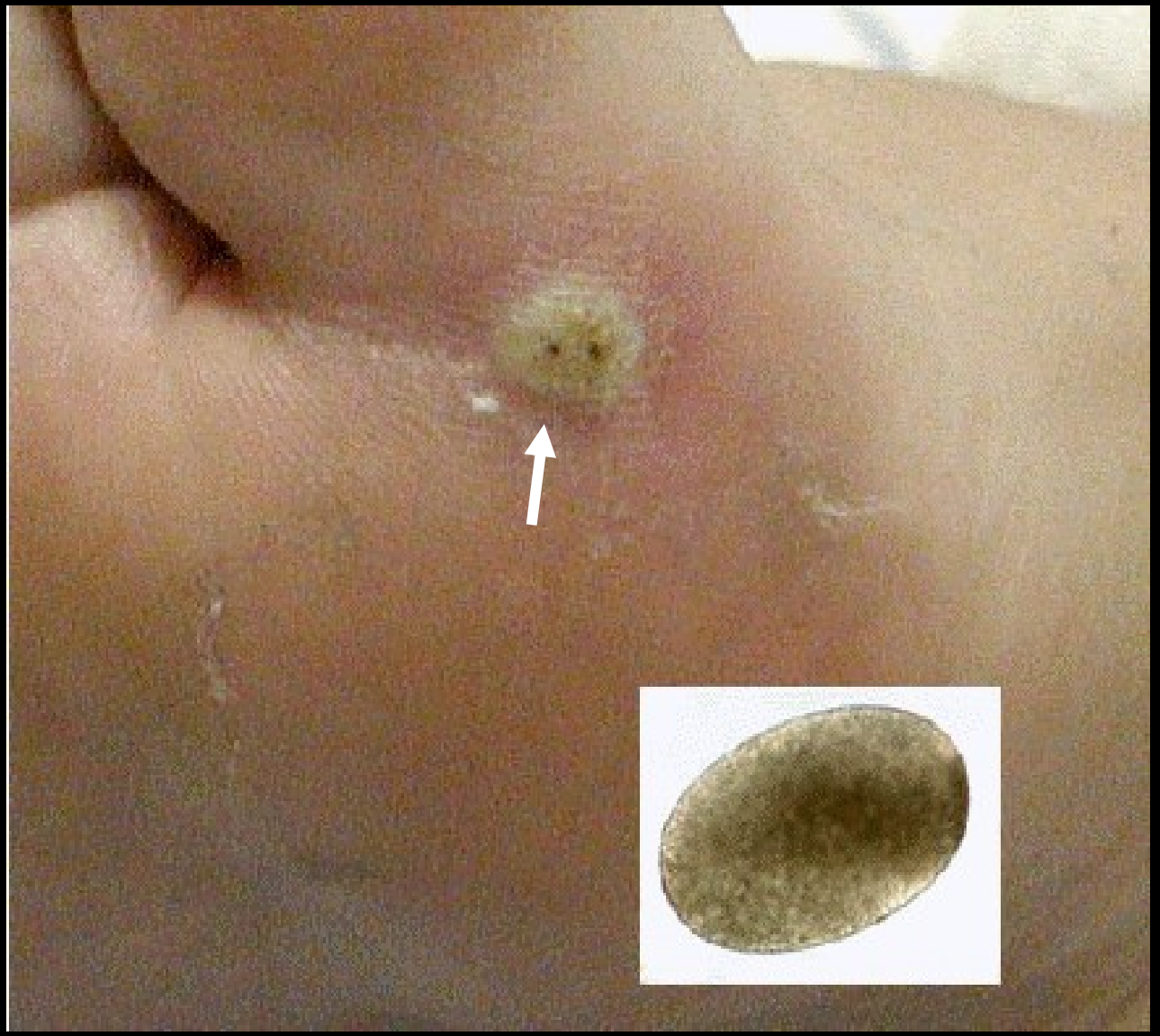
Other

- Drug hypersenitivity reactions
- Phytodermatitis
- Seabathers eruuption
- Viral diseases (varicella, rubella)



A 25 year old female recently returned from a trip to Jamaica. Spent a lot of time on the beach. She presents 1 day after return with a linear eruption on her leg. She remembers seeing both dogs and cats on the beach.

Phytophotodermatitis is a phototoxic eruption following skin contact with an irritant plant substance while in the presence of a systemic photosensitizing compound and ultraviolet radiation. Psoralen, a substance responsible for inducing photosensitization, is found in lemons, limes, bergamot, figs, dill, mustard, parsnip, and garden and wild carrot. Lesions develop hours to days after exposure. Areas of erythema, vesicles, or hyperpigmented plaques develop, often in the form of finger marks or streaks corresponding to sites of plant contact with the skin. Hyperpigmentation resolves over a period of weeks to months




A

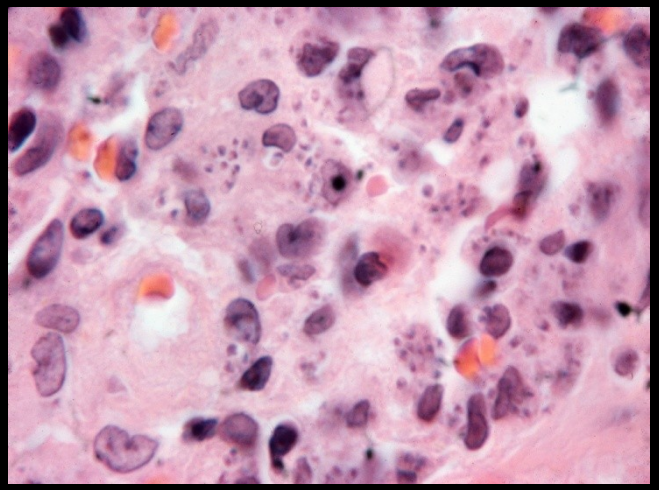

B

Ulcerative Skin Lesions in the Returning Traveler

BACTERIA	
Anthrax	Hermorrhagic, surrounding edema
Chancroid	Painful genital
Lymphogranuloma venereum	Painless genital
Mycobacterium marinum	Nodules that ulcerate
Mycobacterium ulcerans	Deep ulcer
Plague	Breakdown of a lymph node
Pyoderma	Crusted ulcer with Staphylococci
Syphilis	Painless genital with induratioin
Tularemia	Ulcerated nodule
Tropical ulcer	Painful, necrotic
PROTOZOA	
Amebiasis	Rapidly growing, painful necrotic
Leishmaniais	Painless, rolled edge, chronic
OTHER	
Insect bites (Spiders)	Necrotic, painful, edema

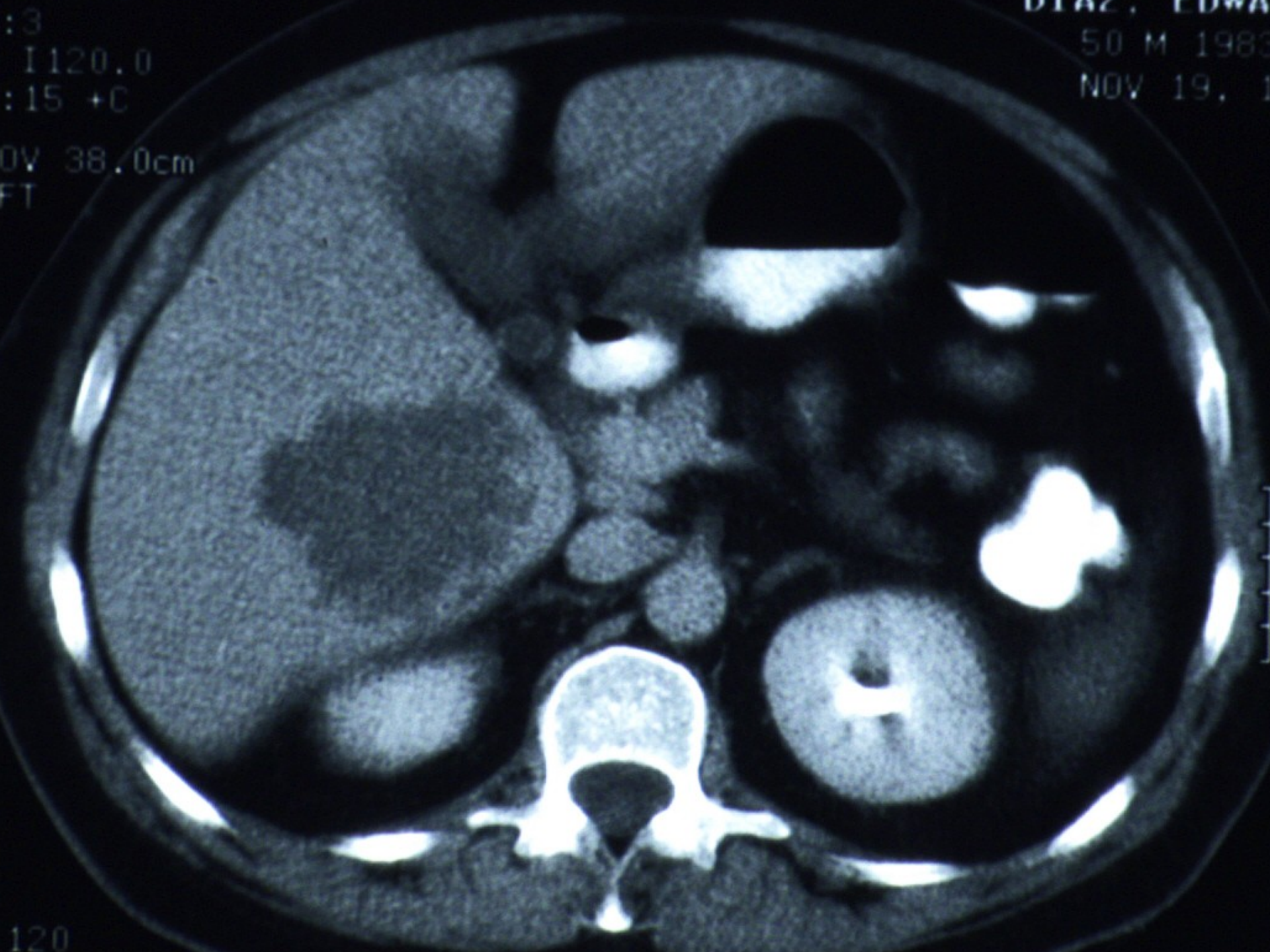
Case Presentation

- 14 year old born in Equador
- Travelled here by boat and car
- Noted papule in Mexico which enlarged
- Ulcerated and grew next 2-3 weeks
- Ulcer painless and remained same
- Physical examination normal except ulcer with rolled borders (seen on next slides) and palpable lymphadenopathy up the arm (arrows)



Case

- The patient is a 30 year old Mexican who immigrated to the US in 1998. He just returned to Mexico for one month and returned two months ago. He now presents with fever (103c) and abdominal pain. He denies history of fever. His physical examination is significant for ruq tenderness. He has a normocytic anemia, no eosinophilia and a slightly elevated alkaline phosphatase. His CAT scan is on the next slide.


:3
I120.0
:15 +C
OV 38.0cm
FT
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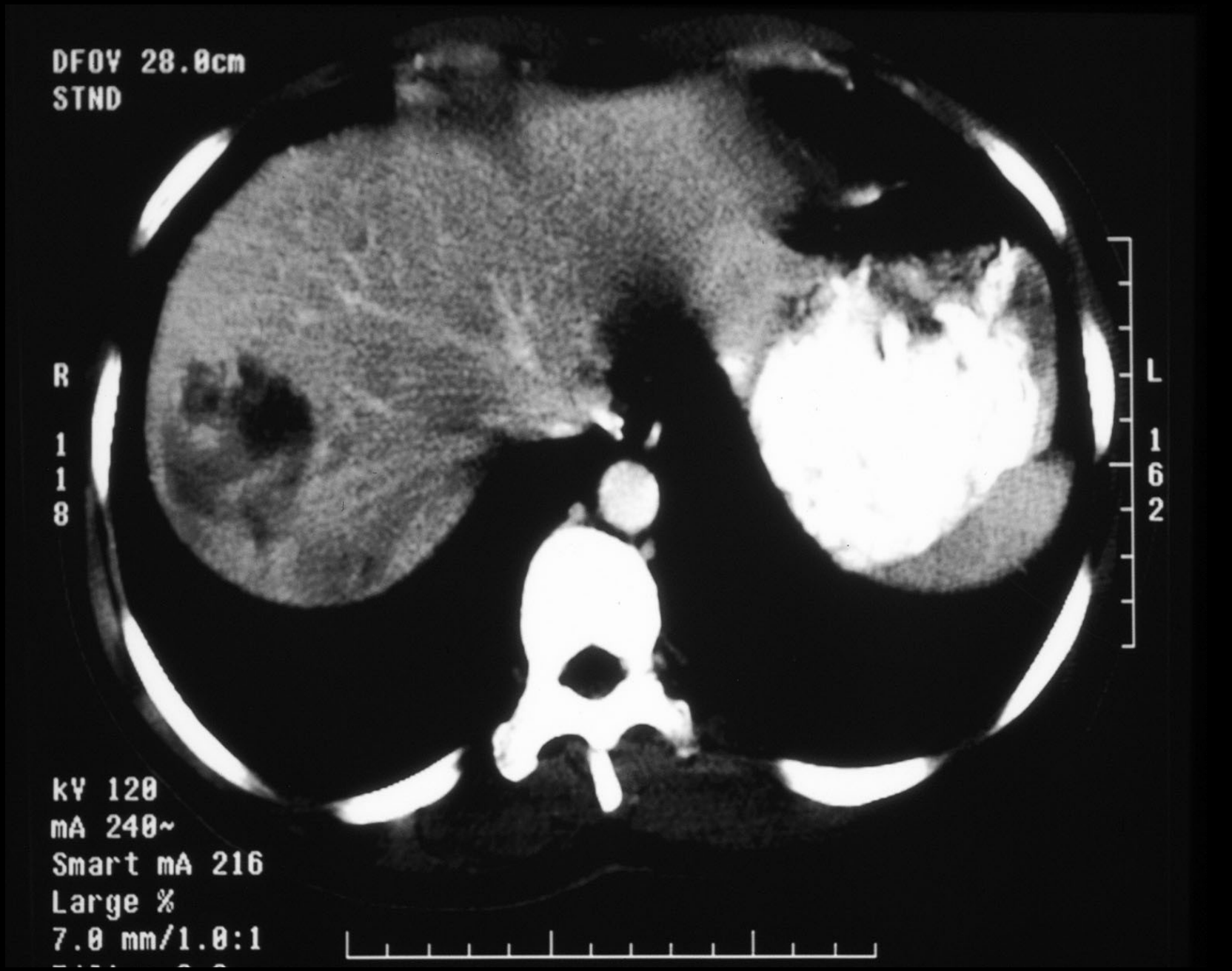
120

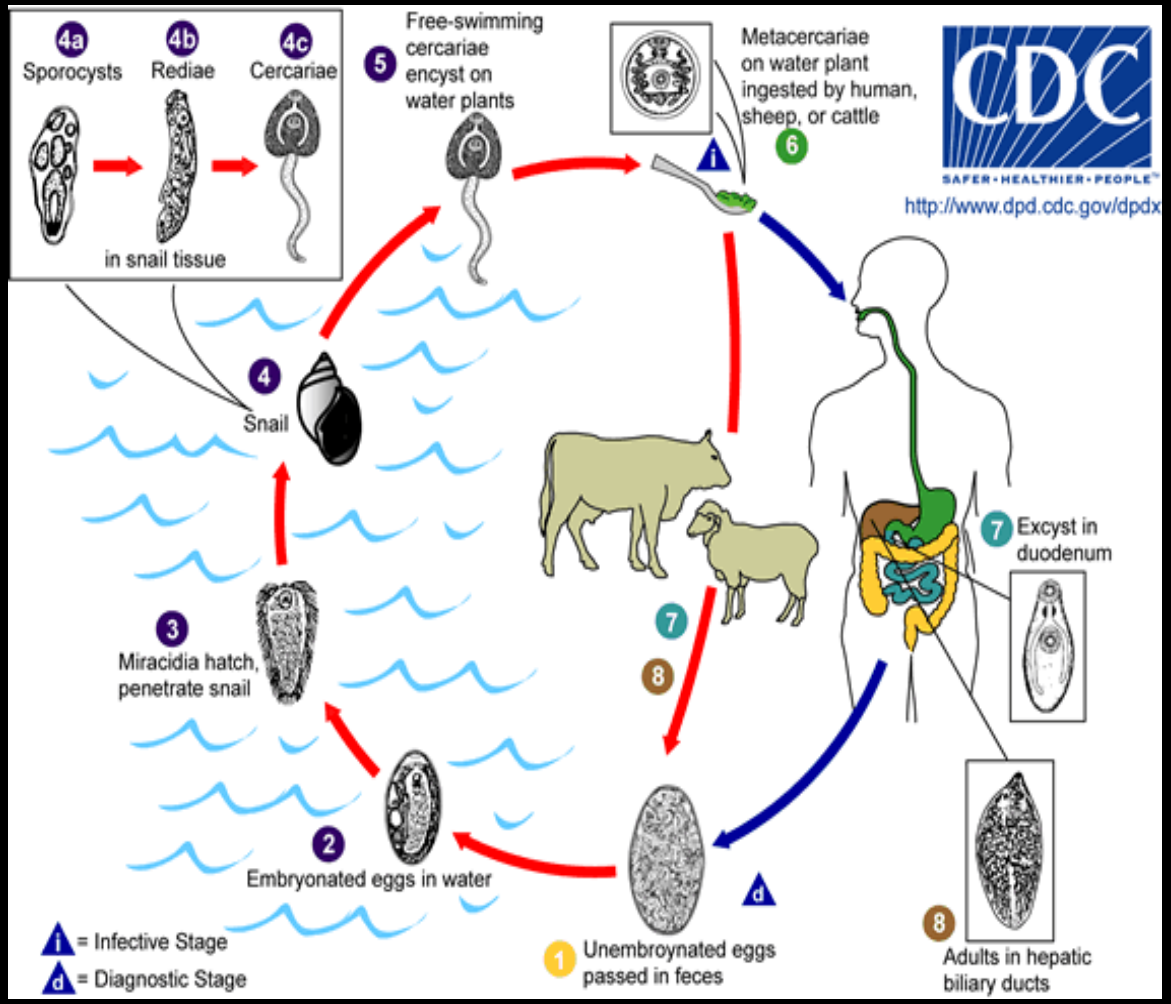
A 26-year-old woman from the Dominican Republic was well on arrival in the United States in late February 1997. One month later she presented to a local hospital complaining of several hours of severe, sharp, right upper quadrant pain radiating to the right shoulder, with fever and chills. She denied a history of gallstones, jaundice, use of nonsteroidal antiinflammatory drugs or oral contraceptives, urinary changes, or recent trauma. On admission to the hospital her temperaturewas normal, and she had mild right upper quadrant tenderness without hepatosplenomegaly or masses. A test result for Beta-human chorionic gonadotropin was negative, and she had peripheral eosinophilia (27%). An abdominal computed tomography (CT) scan with intravenous contrast demonstrated a 6.0 × 5.0 × 4.0 cm complicated, heterogeneous, necrotic mass in the right lobe of the liver, which extended from the dometo the inferior border, and laterally to thecapsule . The mass contained internal septations with surrounding parenchymal hemorrhage. An IgG-enzyme immunoassay result for antibodies to *Echinococcus granulosus* was low positive. The patient was then transferred to our institution for further management.


DFOV 28.0cm
STND
R
118
L
162
kV 120
mA 240~
Smart mA 216
Large %
7.0 mm/1.0:1

She denied exposure to farm animals, dogs, or fresh water. Other family
members were well. She had a temperature of 36.9°C, clear lungs, and no liver tenderness or hepatosplenomegaly.

One week later her white blood cell was 16,800/mm3 with 5,200/ mm3 eosinophils (31%). She had an alkalinephosphatase level of 124 U/liter, an alanine aminotransferase level of 32 U/liter, and a bilirubin level of 0.5 mg/dL. Review of the CT scan revealed the above noted findings, which were considered inconsistent with a hydatid cyst because of the absence of either a capsule or calcification, and the presence of hemorrhage within the cavity. A repeat CT was unchanged.

Results of ameba serology and Western blot for echinococcus were negative, and stool specimens contained *Blastocystis hominis* and *Endolimax nana*. The following week, the eosinophilia count peaked at 7,000/mm3 (46%) and gradually decreased thereafter.



She had frequently eaten uncooked “berro” or watercress (Nasturtium officinale).

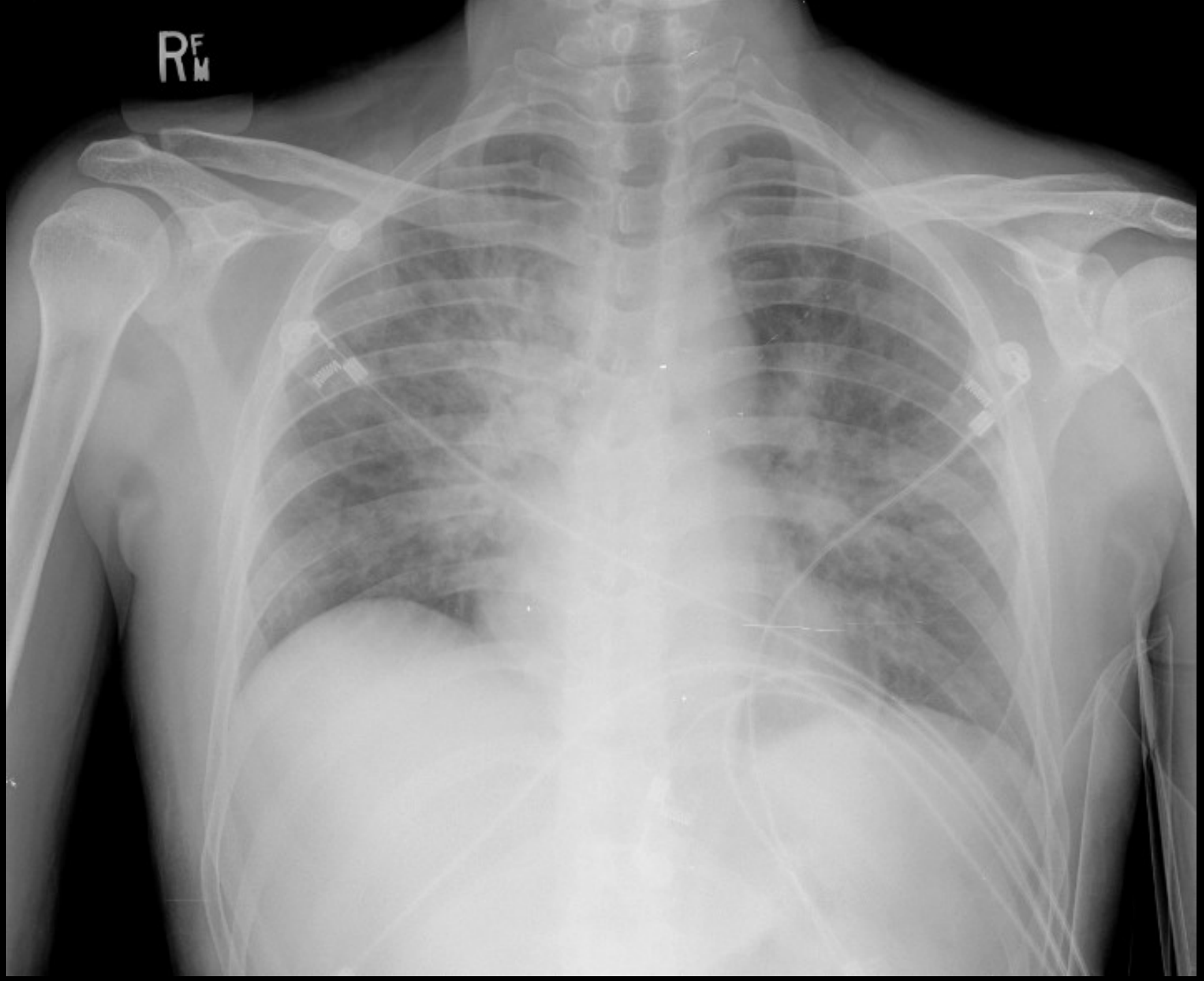
Serum tested negative for antibodies to *Fasciola hepatica* (Falcon assay screening test-enzyme-linked immunosorbent assay [FAST-ELISA]; Departamento de Patologia y Medicina de Laboratoria, Universidad de Puerto Rico, San Juan, PR) on presentation, however, indirect immunofluorescence (IIF) tests for antibodies to Fasciola hepatica performed on serum obtained one and two weeks after the negative FAST-ELISA result revealed increasing titers of 1:80 and 1:160, respectively (1:20 borderlinepositive; LaboratoiredeParasitologie - Mycologie, Groupe Hospitalier Cochin, Paris, France). The result of an immunoelectrophoresis test was also positive,showing three bands on the first serum and four bands on the latter one.

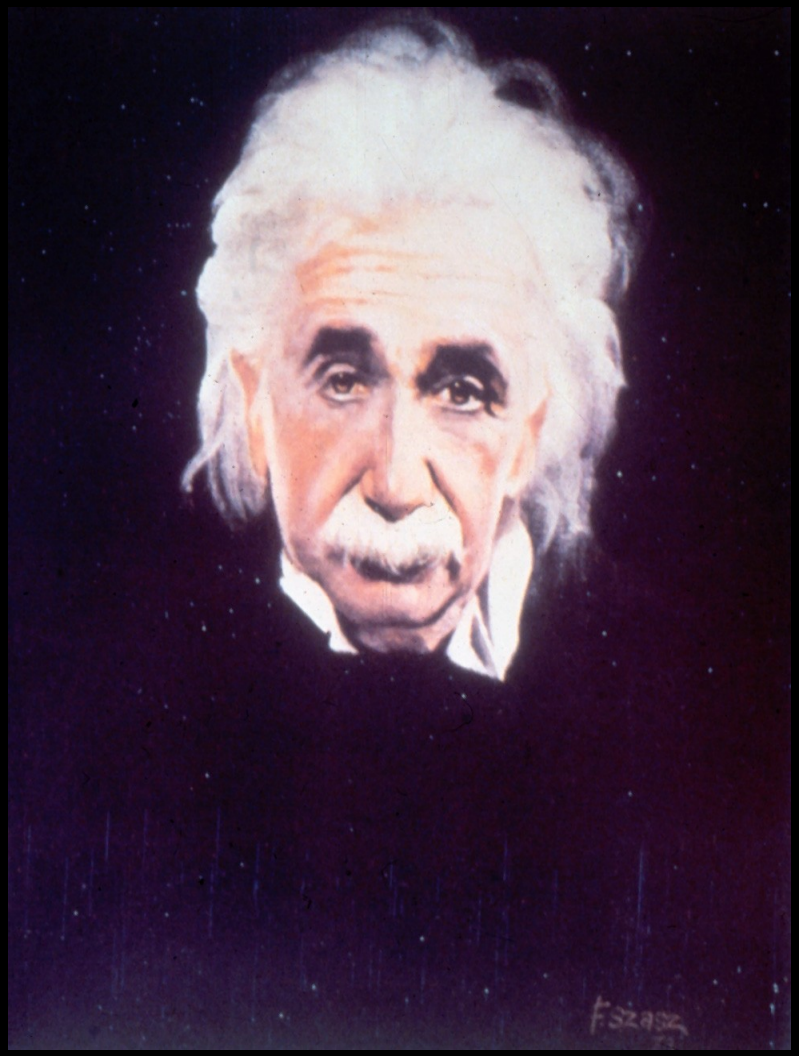
The patient was treated with a single dose (10 mg/kg , 700 mg) of triclabendazole (Fasinex; Novartis, Basel, Switzerland). CT scan 12 weeks later.

Immature flukes perforateGlisson ’s capsule and burrow through the parenchyma, causing focal hepatic necrosis and abscesses. They next invade the bile ducts, mature there in approximately 3-4 months

Case

- 42 year old male with h/o pemphigus vulgaris – originally from Guyana
- Started on steroids (prednisone 100 mg qd) for 6 months
- Admitted June 2006
  - Epigastric pain for 4 days
  - Non-bloody diarrhea (4-5 episodes/day)
  - Pt d/c-ed steroids few days before admission
  - Na+ 124, K 3.1, CO2 25.3, Bun/Cr 13/0.6
  - His CXRY shows bilateral infiltrates – see next image
  - His WBC is 9,000/mm^3 with 89% granulocytes


RF
M

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