A 22-year-old man presents with ten days of fever that started three weeks after returning from visiting family in Bangladesh. He complains of headache, abdominal pains, anorexia, a dry cough and generalised muscular aches and pains.

On examination he looks ill. Temperature is 40.5°C, pulse 92/minute and blood pressure 120/65 mm Hg. On auscultation he has a clear chest. There is generalised abdominal tenderness without rigidity or guarding.

Blood tests show:
- haemoglobin 140 g/L [130-180]
- white cell count 3.5 x 10^9/L [4.0-11.0]

Blood films are repeatedly negative for malaria. Renal function, electrolytes, liver enzymes and chest X-ray are normal.

What is the most likely diagnosis?
A. Acute schistosomiasis.
B. Amoebiasis.
C. Leptospirosis.
D. Typhoid.
E. Dengue fever.

**Evaluation of fever in returning traveler**

**Hx:**
1) What processes might cause febrile illness if individual had not traveled
   - routine infections
   - noninfectious disease that cause fever → thrombophlebitis, PE, drug fever
2) Dates of travel, duration of stay, activities and exposures, vaccinations/prophylactic Ab
3) Sexual history
   - STD tha cause fever: syphilis, disseminated gonococcal infection, HIV, Hep B, CMV, Hep A, Hep C (rare)
4) Vaccines
   - yellow fever and Hep A vaccines are highly efficacious, making infection unlikely
   - some travelers lack immunity to measles, rubella and diphtheria because of gaps of immunization
   - malaria chemoprophylaxis is not 100% effective and may experience resistance.

**Timing of exposure**

If more than a month has lapsed since tropical travel, many infections can be excluded

**Physical examination**

1) Special care for skin lesions
2) lymphadenopathy
3) retinal or conjunctival changes
4) enlargement of liver or spleen
5) genital lesions,
6) neurologic finding

**Investigations**
1) FBE, LFT, blood cultures,
2) blood smears for malaria (done urgently that day)
3) Cxr
4) Urinalysis

In the GeoSentinel study, among patients with systemic febrile illness, the most common specific diagnoses were the following:

- Malaria
- Dengue fever
- Mononucleosis (due to EBV or CMV)
- Rickettsial infection
- Typhoid or paratyphoid fever
General Principles

1) 4 major syndromes:
   a) Systemic febrile illness
   b) Acute diarrhea
   c) Dermatologic disorders
   d) Chronic diarrhea

2) Malaria was the most frequent cause of systemic febrile illness
   Dengue was more frequent in all regions except sub-Saharan Africa and Central America

3) Rickettsial infections appeared most exclusively among travelers returning from sub-Saharan Africa
   Typhoid fever was the leading systemic febrile illness in those returning from South central Asia

4) Parasite-induced diarrhea was more common among travelers than was bacterial diarrhea in all regions except SEA
   In SEA, campylobacter was the predominant pathogen

5) Insect bites were the most common cause of dermatologic complaints
   Cutaneous larval migrans was the most common skin disorder from Caribbean

Acute Schistosomiasis

Majority are completely asymptomatic although acute Sx more common in nonimmune individuals eg. Travelers, because of a more intense immune response to exposure

1) Swimmers itch
   - localized dermatitis that result in a pruritic popular rash at the site of larval entry (lower legs/feet)
   - seen within one day of exposure
   - tingling and itching at site of entry followed by intensely pruritic popular eruption 12-24 hrs later seen in people with repeated contact

2) Katayama fever
   - Sx: fever, chills, myalgias, arthralgias, dry cough, diarrhea and headache
   - signs: lymphadenopathy, hepatosplenomegaly
   - lx: eggs not frequently excreted in detectable amounts but peripheral eosinophilia will be present
   - develop between 4 to 8wks after exposure
   - due to hypersensitivity to schistosome antigens and circulating immune complexes
   Sx more likely to occur in travelers and other non immune hosts.

Amebiasis

Caused by protozoan Entamoeba histolytica
2 other strains E dispar and E moshkovskii (asymptomatic)
Parasite exists in 2 forms : 1) cyst stage (infective) 2) trophozoite stage (invasive disease)
Infection occurs following
a) ingestion of amebic cysts via contaminated food or water
b) venereal transmission through fecal-oral contact

Areas with high rates of amebic infection:
India, Africa, Mexico, parts of Central and South America

Pathway
Cysts pass through stomach to small intestine when they excyst to form trophozoites. Trophozoites invade and penetrate the mucous barrier of the colon causing tissue destruction and increased intestinal secretion. Cause bloody diarrhea.

**Clinical manifestations**

Subacute onset:
1 - 3 weeks
Sx: mild diarrhea to severe dysentery producing abdo pain, diarrhea and bloody stools.
   - Weight loss (<50%)
   - Fevers (8 - 38%)
   - Fulminant colitis with bowel necrosis leading to perforation and peritonitis (0.5%)
Ass with mortality rate of > 40%

Chronic:
Present as chronic, nondysenteric syndrome of diarrhea, weight loss and abdo pain over years
Asymptomatic

**Diagnosis**

1) Microscopy of stools
   - to show cysts or trophozoites.
   - Cannot differentiate between 3 strains
2) Antigen testing *BEST*
   ELISA test specific for E histolytica
3) Serology
   - Antibodies detectable within 5-7 days of acute infection
   - Indirect hemagglytination is the most sensitive assay and is +ve to app 90% of pts with symptomatic intestinal infection

**Treatment**

E.dispar and E.moshkovskii infection does not require treatment
Asymptomatic E. histolytica show be treatmed because of potential risk of developing invasive disease and risk of spread to family members

1) Metronidazole (500-750mg tds for 7-10 days)
   - 90% success rate
2) Tinidazole
   - 2g oral daily for 3 days
   - 90-93% cure rate
   PLUS
If patients have invasive colitis, they should be treated with agents for eliminating luminal cysts

1) Paromomycin
2) Diiodohydroxyquin

Follow up stool examinations are required after completion of therapy

**Leptospirosis**

(Synonyms: Weil's disease, Swineherd's disease, rice-field fever, cane-cutter fever, swamp fever, mud fever, hemorrhagic jaundice, Stuttgart disease and Canicola fever)

Zoonosis with protean manifestations cause by spirochete, Leptospira interrogans
Spiral shaped
Aerobic spirochetes with 18 or more coils per cell

**Epidemiology**
Majority of clinical cases occur in tropics
Man is incidentally infected after exposure to environment contaminated by animal urine, contaminated urine or via aerosola

**Clinical manifestation**
Non specific clinical illness
Disease may manifest as a subclinical illness followed by seroconversion, a self limited systemic infection or a severe, potentially fatal illness accompanied by multiorgan failure

Incubation period: 2-26days (average 10d)
Abrupt onset of fever, rigors, myalgias and headache (75-100%)
Non productive cough (25-50%)
Nausea, vomiting and diarrhoea (50%)
Less common Sx: arthralgias, bone pain, sore throat, abdo pain

Complications:
Most cases are mild to moderate
Course may be complicated by: Renal failure, uveitis, haemorrhage, acute respiratory distress syndrome, myocarditis, rhabdomyolysis

**Diagnosis**
Cluture:
blood and CSF specimens are +ve during the 1st 10d of illness
Isolation of organisms from blood is successful in about 50% of cases
Urine becomes +ve during the 2nd week of illness and remain so for up toe 30d after resolution of symptoms

Microscopy: Stains with dark field microscopy, silver stain or fluorescent microscopy
Culture: in 1-2 weeks or may take up to 3 months

Serology:
Used for confirmation
GOLD STANDARD: Microscopic agglutination test (MAT)
More specific when a 4 fold or greater rise in titer is detected between acute and convalescent serum specimens
A single titer of > 1: 800 is a strong evidence of current or recent infection

Other Ix:
WCC < 10,000
Urinalysis: freq shows proteinuria, pyuria, granular casts and occasionally microscopic hematuria
Elevated CK - 50%
Elevated hepatic transaminases (40%)
Hyponatremia in severe leptospirosis
Cxr: (MAY SHOW) small nodular densities which can progress to confluent consolidation or ground glass appearance

**Treatment**
1) self - limiting
2) doxycycline
   - for outpatients because it is also effective for rickettsial disease (often confused with leptospirosis
   - dose: 100mg bd
Typhoid fever

Organism: Salmonella typhi or Salmonella paratyphi A, B, or C
- Gram -ve bacilli

S.parathypi A: more likely to be nalidixic acid and fluoroquinolone resistant compared to S.typhi
Spread via ingestion of contaminated food or water
High risk areas: India subcontinent

Presentation: (AGAIN VARIABILITY IN MANIFESTATIONS)
1st week: rising "stepwise" fever and bacteremia
2nd week: abdo pain and rash (rose spots, which are faint salmon colored macules on trunk and abdomen)
3rd week: hepatosplenomegaly, intestinal bleeding and perforation related to ileocecal lymphatic hyperplasia of the Peyer's patch - occur with secondary bacteremia and peritonitis

Diagnosis:
- Blood cultures: +ve in 40-80% of patients
- Stool culture: +ve in up to 30-40%, often -ve
- Bone marrow- often diagnostic
- Blood test:
  - Anemia
  - Leukopenia/ leukocytosis
  - Abnormal LFT (suggestive of acute viral hepatitis)

Prevention:
- Typhoid vaccination- does not provide protection against paratyphoid fever and neither is completely effective against S.typhi
- Caution in what is ingested

Treatment:
- Complicated by development and rapid dissemination of typhoidal organisms resistant to ampicillin, trimethoprim-sulfamethoxazole and chloramphenicol
  1) Ciprofloxacin (500mg bd) for 7 - 10days
  2) Ceftriaxone (2-3g daily) for 7-10days

Alternatively:
1) Azithromycin
2) Chloramphenicol

Dengue fever
Year 2005 Paper two: Questions supplied by Ilynn

Transmitted by Aedes aegyptii mosquito
Virology: DEN-1, DEN-2, DEN-3, DEN-4 of genus Flavivirus

Incubation period of 4-7 days
But can be excluded if more than 14 days after returning

**Clinical presentation:**

1) Asymptomatic infection
   - younger the age, the less symptomatic (Sx less frequent in < 19yo)

2) Self limited dengue fever
Dengue hemorrhagic fever with shock syndrome
   - risk of severe disease higher in sequential infection

3) Classic dengue
   - fever, headache, retroorbital pain, marked muscle and joint pains
   - fever last 5 - 7 days
   - develop biphasic (saddleback) fever curve
   - febrile period followed by period of marked fatigue that can last for days to weeks
   - rash occurred between 2 and 5 days after onset of fever

Other Sx:
Fever 90%
Headache, eye pain, body pain & joint pain (63-78%)
Rash (>50%)
GIT Sx - N + V (>50%)
Diarrhea (30%)
Resp Sx - cough sore throat, nasal congestion (33%)

4) Dengue haemorrhagic fever
   - 4 cardinal features by WHO
     a) Increased vascular permeability (plasma leakage syndrome) - haemoconcentration, pleural effusion, ascites
     b) Marked thrombocypenia ( < 100,000)
     c) Fever lasting 2 - 7 days
     d) Haemorrhagic tendency or spontaneous bleeding

5) Dengue shock syndrome

**Physical examination:** non-specific
Macular or maculopapular rash in 50%

**Diagnosis**
A CLINICAL one in endemic countries
Serology test:
-- IgM immunoassay (MAC-ELISA) - yield a false negative result if obtained within the 1st 6 days of illness
-- To confirm +ve IgM assay result, a convalescent phasae serum sample should be obtained 10-14 days after the acute phase serum
Acute and convalescent specimens analysed together by a hemagglutination inhibition (HI) to provide definitive serologic testing

**Treatment:**
Supportive treatment
1) IV replacement due to plasma leakage
2) Blood transfusion if significant bleeding

Sx in patients with dengue resolve in 5-7 days
Back to Question:

The 2 most likely diagnosis is Dengue and typhoid from the general principles for someone with fever returning from Asia. The incubation period is the differentiating factor here as he presents 3 weeks after returning. Dengue fever can be excluded if presents after 2 weeks. Abdo pain is also a less common symptom of Dengue fever but hey who knows with these infectious disease, they kinda could get anything really.

Leptospirosis could be very likely as well as it fits all the description. Incubation period is around 3 weeks, presents with fever, abdo pain and can have leucopenia. Why it isn't the answer, I don't know. But the question does say MOST FREAKING LIKELY.

Therefore the answer is D Typhoid.