QUESTION 67

A 26yo man presents with a 2 day history of fevers, rigors, headache, malaise, nausea and vomiting, dry cough, mild arthralgia and backache. He reports no shortness of breath, diarrhoea, neck stiffness or photophobia. He reports that he returned from a diving trip to the Solomon Islands seven days ago. He has taken doxycycline regularly as malarial prophylaxis.

On day 3 after the onset of the illness he develops a rash over his trunk (shown below) and face. A petechial rash was noted on his lower limbs.

Which of the following is the most likely diagnosis?

A. Malaria  
B. Dengue fever  
C. Typhoid fever  
D. Q fever  
E. Measles

This picture is not really very helpful in making the diagnosis. He has a maculopapular rash which could occur with just about anything. It is important to note that he also has a petechial rash on his legs which was surreptitiously slipped in at the end of the question. This is only associated with dengue fever.

DENGUE FEVER

- Incubation period is 3 to 7 days (maximum 14 days)  
- Should be suspected in travelers who have returned to Australia in the last week  
- Can also occur in far North Queensland and NT  
- Transmitted by mosquitoes  
- There are 4 viral serotypes, all flaviviruses with single stranded enveloped RNA (DEN-1 to DEN-4)  
- Infection with one serotype confers life-long immunity to that serotype but not the others  
- Infection with a second serotype at any time can lead to dengue haemorrhagic fever
HISTORY

- Fever (typically begins on day 3, occasionally falls after 2-4 days and then returns 24 hours later = saddleback fever)
- Can exclude dengue in a traveler returned > 14 days ago
- Headache, retroorbital pain
- Myalgia, arthralgia
- Rash
- Nausea, vomiting, abdominal pain
- Malaise
- Cough, sore throat
- Haemorrhagic manifestations (more common in DHF but also occur in DF) eg: purpura, epistaxis

EXAMINATION

- Fever
- Rash (maculopapular)
- Conjunctival injection
- Pharyngeal erythema
- Lymphadenopathy
- Hepatomegaly

INVESTIGATIONS

- Leukopaenia
- Thrombocytopaenia
- Elevated AST

DENGUE HAEMORRHAGIC FEVER

- Four cardinal features:
  o Increased vascular permeability evidenced by haemoconcentration (20% or greater rise in haematocrit above baseline), pleural effusion or ascites
  o Marked thrombocytopaenia (< 100)
  o Fever lasting 2 to 7 days
  o Haemorrhagic tendency (as demonstrated by a positive tourniquet test) or spontaneous bleeding (can also occur with DF)
- Dengue shock syndrome is when shock is present along with these four criteria

DIAGNOSIS

- Mainly clinical
- IgM (can get false negatives in first 6 days of illness), should test convalescent sample also to confirm diagnosis

TREATMENT

- No specific treatment for DF
- Avoid NSAIDS or aspirin due to thrombocytopaenia
- In DHF, need aggressive fluid resuscitation, blood transfusion
MALARIA

- 600 to 800 cases a year in Australia
- Mostly in returned travelers (but not exclusively)

PARASITES

- Four species of malaria:
  - Plasmodium falciparum (potentially lethal)
  - Plasmodium malariae (can persist in circulation of > 20yrs)
  - Plasmodium vivax (commonest, relapses from dormant liver stages months to years after infection)
  - Plasmodium ovale (least common, can also relapse)
- All species cause influenza-like symptoms with fever and anaemia
- Serious complications occur only with falciparum (e.g., cerebral malaria, ARF, shock)
- Begins with mosquito bite when sporozoites are injected
- Sporozoites are rapidly passed to the liver where they multiple before bursting the infected cells and releasing thousands of merozoites into the circulation
- Merozoites invade RBCs
- Mature and undergo asexual division (schizogony) into schizonts
- Schizonts burst the infected cell and release daughter merozoites that can invade other RBCs
- Hepatic infection (5 days to several weeks) is asymptomatic
- Typical symptoms of malaria occur at the time of schizont rupture when parasite toxins act on host cells to release cytokines
- P. falciparum alters the surface of infected RBCs causing them to adhere to endothelial cells in various capillary beds as they mature
- When sequestration occurs in the brain, lung, gut, placenta or kidney can cause serious problems
- Also can make diagnosis difficult as parasite may be undetectable in peripheral blood at this time
- At some time during replication, sexual forms are produced that can be taken up by a feeding mosquito and fertilized in the mosquito midgut → sporozoites in salivary glands → transmission to other humans

CLINICAL MANIFESTATIONS

- Fever in a returned traveler to endemic area = malaria until proven otherwise
- Rigors
- Malaise
- Headache
- Vomiting and diarrhoea may occur
- Cough
- Rash not a feature
- Fever occurring less than 1 week after reaching endemic area is very unlikely to be malaria
- Falciparum usually occurs within 4 weeks of leaving endemic area (but can be later)
- Vivax and ovale can relapse years later

SEVERE MALARIA (FALCIPARUM)

- Can progress rapidly to ARF, ARDS, severe metabolic acidosis, DIC, shock or cerebral malaria
Year 2004 Paper two: Questions supplied by Megan

- Neurological symptoms in cerebral malaria – seizures, hypertonicity, gaze palsies, delirium, psychosis or coma
- Severe malaria =
  - Any degree of altered consciousness, jaundice, oliguria, severe anaemia or hypoglycaemia
  - A parasite count about 100,000/mm³ (>2% RBC parasitized)
  - Patient is vomiting or clinically acidic

**DIAGNOSIS**

- Thick and thin smear of peripheral blood is gold standard
- Thick smear is to concentrate the parasites, species diagnosis best made on thin film
- Single negative smear does not exclude malaria, repeat if clinical suspicious high (every 8 – 12 hours)
- Thrombocytopenia common
- CSF is normal in cerebral malaria
- Patients from malarious areas who are semi-immune may have parasites in their blood but this may not be the cause for their fever

**TREATMENT**

- All patients with falciparum need admission and close monitoring for complications
- Pts with other species can be treated as outpatients if not unwell

**Vivax, Ovale and Malariae:**

- P. vivax, P. ovale and P. malariae are treated with chloroquine
- Chloroquine resistance reported in PNG, Indonesia, SE Asia
- Chloroquine resistance: artemether + lumefantrine or mefloquine or quinine are alternatives
- Primaquine is used for P. vivax and P. ovale to reduce the possibility of relapse (but does not eliminate risk)
- All patients who are to receive primaquine must be tested for G6PD deficiency as this drug can cause lysis of RBCs
- Patients who have relapses despite primaquine may need repeated course or higher doses

**Uncomplicated Falciparum:**

- P. falciparum is treated with artemether + lumefantrine
- Alternatives are doxycycline or clindamycin
- OR atovaquone + proguanil
- OR mefloquine
- Atovaquone + proguanil and mefloquine should not be used for treatment of malaria in patients who took these drugs as prophylaxis

**Severe Malaria:**

- Assume infective species to chloroquine-resistant falciparum
- Artesunate IV is first choice
- Alternative is quinine IV (if artesunate not immediately available) beginning with a loading dose
- Do not give loading dose if patient has received 3 or more doses of quinine or quinidine in the previous 48 hours or if mefloquine prophylaxis has been used in the previous 24 hours or a mefloquine treatment dose within the last 3 days
- Need to monitor BSL with quinine as it stimulates insulin secretion
- Cardiac monitoring is also advised if there is pre-existing heart disease (quinine can cause arrhythmias)

**MONITORING**

- Parasite count every 12-24 hours (may rise initially) until all parasites are cleared
- IV should be changed to oral antimalarial as soon as possible
- Treat with oral quinine plus doxycycline or clindamycin for total of 7 days of quinine

**PREVENTION**

- For areas with chloroquine-sensitive malaria – chloroquine
- For areas with chloroquine-resistant malaria – mefloquine or doxycycline
- For areas with mefloquine-resistant malaria - doxycycline

**TYPHOID**

- Can clinically mimic malaria
- Caused by salmonella typhi (or salmonella paratyphi → paratyphoid)

**CLINICAL FEATURES**

- Incubation period 5 to 21 days
- Fever, chills (classical rising fever and bacteraemia in first week)
- Abdominal pain (classically in 2nd week)
- Headache
- Rash – faint rose spots on trunk (week 2)
- Hepatosplenoengaly, GI bleeding/perforation (3rd week)
- Diarrhoea not common
- Sepsis, altered conscious state
- Relative bradycardia (ie. High temperature but low normal HR)

**DIAGNOSIS**

- Blood cultures (positive in 40 to 80%)
- Stool culture (30 to 40%)
- BM aspirate has much higher sensitivity, even after antibiotic treatment
- Anaemia
- Leukopaenia > leukocytosis

**TREATMENT**

- Ciprofloxacin 500mg orally bd for 7 to 10 days
- If cipro resistant use Ceftriaxone or azithromycin
MEASLES

- Characterised by 3 to 4 days of fever, cough, coryza and conjunctivitis
- Followed by rash which starts on face and neck and spreads downwards
- Koplik spots (small white spots inside the cheek) appear 1-2 days before the rash and are pathognomonic
- Supportive treatment
- Rare but potentially serious complications include bacterial superinfection, measles pneumonia, post-infectious encephalomyelitis and subacute sclerosing panencephalitis

Q FEVER

- Q fever not associated with a rash
- Classically presents as fever in an abattoir worker
- Can be acute or chronic relapsing
- Treatment is oral doxycycline