SELF-ASSESSMENT QUESTIONS

MILITARY TROPICAL MEDICINE

MS Bailey[1,2], CJ Ellis[2]

[1]Department of Military Medicine, Royal Centre for Defence Medicine, Birmingham, UK. [2]Department of Infection & Tropical Medicine, Birmingham Heartlands Hospital, UK.

Abstract

Tropical diseases remain a significant threat to deployed military personnel as demonstrated by recent outbreaks amongst troops in Sierra Leone, Iraq and Afghanistan. Five cases are presented from military deployments in tropical or sub-tropical areas, which illustrate important diseases and diagnostic principles for military physicians.

Case 1

An 18-year old infantry soldier presents with a 3-week history of a "boil" on his right elbow (Figure 1). It is painful and there is a continual leak of blood-stained serous fluid from the central punctum, which becomes purulent intermittently. Despite treatment with co-amoxiclav and then clindamycin, the lesion has continued to expand. The patient had taken part in a jungle warfare training exercise in Belize 2 months previously.

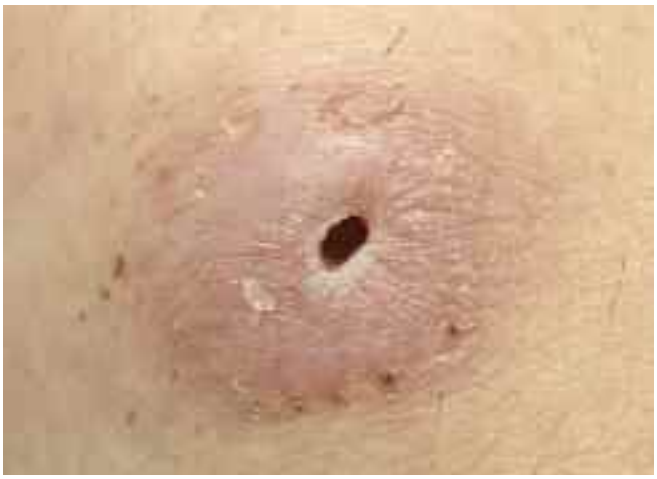

Figure 1. Lesion on right elbow.

Question 1

a. What is your differential diagnosis at this stage ?

b. How would you further examine this lesion ?

c. What is the most likely diagnosis and how is this disease transmitted ?

d. How would you treat such a lesion ?

Case 2

A 34-year old Army nurse presents with a 2-week history of fever each evening associated with night sweats, malaise and anorexia, but no focal symptoms. He had returned from a 12-month deployment in Sierra Leone 3 months previously. Whilst in Sierra Leone he had travelled widely, which required him to consume local food and water on occasions and he reports a few episodes of gastroenteritis during this deployment. He had occasional mosquito bites, but took malaria prophylaxis throughout and received all the recommended vaccines for Sierra Leone. He was also bitten by a dog, but was treated with a full course of rabies post-exposure prophylaxis vaccines. He denies any sexual activity or other exposure to blood-borne viruses during his deployment. On examination he looks unwell and sweaty, but there are no other abnormal physical signs. Initial blood investigations are shown in Table 1. Daily malaria investigations (using thick and thin blood films and antigen-detection tests) for 3 days and cultures of blood, faeces and urine are all negative. A chest radiograph (CXR) is also normal.

Hb (g/dl)	**11.8 (↓)**	Albumin (g/l)	36
MCV (fl)	94	Protein (g/l)	**82 (↑)**
WCC (x10^9/l)	**14.7 (↑)**	Globulin (g/l)	**46 (↑)**
Neuts (x10^9/l)	**11.6 (↑)**	Bilirubin (µmol/l)	7
Platelets (x10^9/l)	**448 (↑)**	ALT (U/l)	**48 (↑)**
ESR (mm/hr)	**119 (↑↑)**	AST (U/l)	**84 (↑)**
CRP (mg/l)	**248 (↑↑)**	ALP (U/l)	**136 (↑)**
Clotting	Normal	GGT (U/l)	**146 (↑)**
U&E	Normal	Ferritin (µg/l)	**1178 (↑↑)**

Table 1. Blood investigations for Case 2 (abnormal values in bold - ↓/↓↓= mildly / moderately low; ↑/↑↑= mildly / moderately elevated)

Question 2

a. What is your differential diagnosis at this stage ?

b. What further investigations should be performed ?

c. What is the most likely diagnosis and how should this be treated ?

Case 3

A 28-year old paratrooper presents with a 1-week history of fever and a 5-day history of upper abdominal pain, nausea, icterus, jaundice and dark urine. He had returned from Afghanistan 6 weeks previously, where he was based at a remote Forward Operating Base (FOB). He denies any consumption of local food or water or any exposure to blood-borne viruses whilst in Afghanistan, but had eaten out regularly and travelled to Spain whilst on post-operational tour leave (POTL). He had received all his usual military vaccinations and taken malaria chemoprophylaxis whilst deployed. On examination he has marked icterus and jaundice and tender hepatosplenomegaly, but no other abnormal physical signs. Initial blood investigations are shown in Table 2. Daily malaria investigations for 3 days, blood

Corresponding Author: Major Mark S Bailey RAMC, SpR in Infectious Diseases & Tropical Medicine, Department of Military Medicine, Royal Centre for Defence Medicine, Vincent Drive, Birmingham, B15 2SQ

Email: mark@ramc.org

cultures and serology tests for hepatitis A, B and C viruses are all negative. Investigations for arboviruses and rickettsiae from Afghanistan are also negative. A CXR is normal and an USS confirms moderate hepatosplenomegaly (with the spleen measuring 19 cm in length), but no other abnormalities.

Hb (g/dl)	13.7	Albumin (g/l)	36
WCC (x10^9/l)	**24.7 (↑↑)**	Protein (g/l)	70
Neuts (x10^9/l)	2.8	Globulin (g/l)	34
Lymphs (x10^9/l)	**14.5 (↑↑)**	Bilirubin (µmol/l)	**140 (↑↑)**
Platelets (x10^9/l)	310	ALT (U/l)	**145 (↑)**
ESR (mm/hr)	**24 (↑)**	AST (U/l)	**242 (↑)**
CRP (mg/l)	**19 (↑)**	ALP (U/l)	**695 (↑)**
Clotting	Normal	GGT (U/l)	**503 (↑)**
U&E	Normal	Ferritin (µg/l)	**1317 (↑↑)**

Table 2. Blood investigations for Case 3 (abnormal values in bold - ↓/↓↓= mildly / moderately low; ↑/↑↑= mildly / moderately elevated)

Question 3

a. What is your differential diagnosis at this stage ?

b. What further investigations should be performed ?

c. What is the most likely diagnosis and what advice should be given ?

Case 4

A 38-year old jungle warfare instructor presents with a 1-week history of fever, headache, non-productive cough, nausea, diarrhoea, myalgia and an erythematous rash. His recent travel history includes deployments in Iraq and Afghanistan, exercises in Brunei and Guyana and a recent holiday in Thailand. On examination he is found to be febrile (38.2 ºC) with a pulse of 64 beats / minute and has a blanching erythematous rash, but no other abnormal physical signs. Initial blood investigations are shown in Table 3. Daily malaria investigations for 3 days and cultures of blood, faeces and urine are all negative. A CXR and abdominal USS are also normal.

Hb (g/dl)	14.8	Albumin (g/l)	37
WCC (x10^9/l)	**2.2 (↓)**	Protein (g/l)	63
Neuts (x10^9/l)	**1.0 (↓)**	Globulin (g/l)	26
Lymphs (x10^9/l)	**0.4 (↓)**	Bilirubin (µmol/l)	11
Platelets (x10^9/l)	**97 (↓)**	ALT (U/l)	**190 (↑)**
ESR (mm/hr)	18	AST (U/l)	**174 (↑)**
CRP (mg/l)	4	ALP (U/l)	**150 (↑)**
Clotting	Normal	GGT (U/l)	**145 (↑)**
U&E	Normal	LDH (U/l)	**560 (↑)**

Table 3. Blood investigations for Case 4 (abnormal values in bold - ↓/↓↓= mildly / moderately low; ↑/↑↑= mildly / moderately elevated)

Question 4

a. What is your differential diagnosis at this stage ?

b. What further investigations should be performed ?

c. What is the most likely diagnosis ?

Case 5

In Iraq, a 26-year old Army driver presents with a 5-day history of fever, polyarthalgia with associated joint stiffness and "bruising" on the anterior aspect of his lower limbs. He reports several insect bites and thinks that his problems are mostly due to sleeping on the ground in rough terrain. On examination he is found to be febrile (38.0 ºC) with a polyarthritis affecting his hands, wrists, knees and ankles and the "bruised" areas of skin are thickened and raised in comparison to the normal surrounding skin (Figure 2).

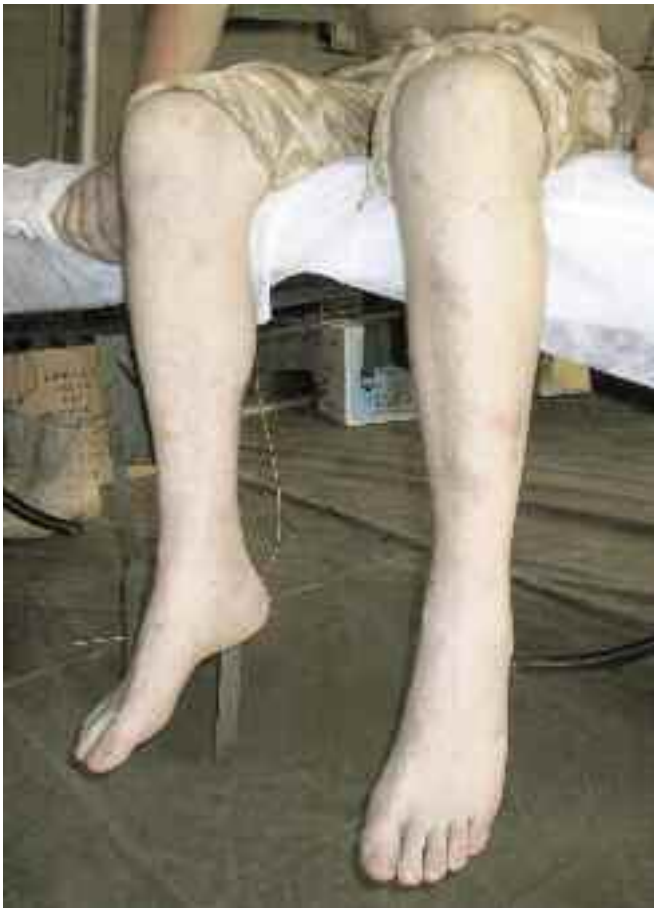

Figure 2. "Bruising" on the shins.

Question 5

a. What is the condition shown in Figure 2 and what may it be associated with ?

b. What further investigations should be performed ?

Answers

Answers for Case 1

a. The differential diagnosis should include a furuncle, abscess, epidermal (sebaceous) cyst and possibly cutaneous leishmaniasis. However, the clinical features of this lesion are most typical of cutaneous myiasis due to a larval infestation.

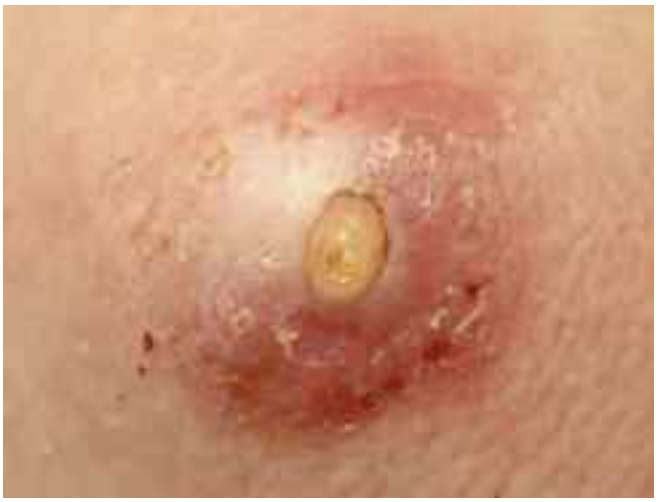

Figure 3. Larva visible with patient's elbow flexed.

b. Prolonged observation, manipulating the lesion or asking the patient to flex his elbow should enable the contents of the cavity to be observed and so confirm that this is a form of myiasis (Figure 3). Alternatively, the punctum can be occluded with petroleum jelly, which will suffocate the larva and cause it to extend its breathing apparatus out of the cavity.

c. There are 2 common forms of human myiasis in Latin America. This case is most likely to be caused by the botfly *(Dermatobia hominis)* because the more troublesome screw-worm *(Cochliomyia hominivorax)* has been eradicated from many Latin American countries – including Belize. Botflies are relatively large flies and usually lay their eggs on other vectors (eg. mosquitoes) to increase the chance of them coming into contact with mammalian skin.

d. Ultimately, the larva and its cavity will enlarge until the punctum becomes large enough to allow it to drop out and complete the remainder of its life cycle. However, this typically takes from 1-3 months and so intervention to remove the larva is recommended. Numerous home-made remedies exist including the use of various materials to occlude the punctum, which may lead to the larva emerging. However, a minor surgical procedure is often necessary due to the small size of the punctum in relation to the larva (Figure 4). The residual cavity normally heals without further problems [1].

Figure 4. Cruciform incision and removal of botfly larva.

Answers for Case 2

a. This is a classical case of (tropical) fever of unknown origin (FUO), which has a wide differential diagnosis initially. However, once UK-acquired infections are excluded, then the prolonged incubation period can narrow the differential diagnosis significantly. Following travel to Sierra Leone and a 3-month incubation period, the most likely diagnoses are malaria (probably non-falciparum), human immunodeficiency virus (HIV) infection, amoebic liver abscess, disseminated tuberculosis (TB) or possibly acute schistosomiasis. The initial blood investigations are suggestive of a significant non-viral infection and the neutrophilia makes an amoebic liver abscess most likely overall. Non-infectious alternatives would include rheumatological conditions such as adult-onset Still's disease, but this would normally present with arthralgia or a rash in addition to the fever.

b. Serology tests for HIV infection, amoebiasis and schistosomiasis should be performed. Further investigations should also include imaging of the abdomen and an ultra-sound scan (USS) revealed a hyper-echoic lesion in the left lobe of his liver, which was imaged in more detail by a CT scan and thought to be an evolving abscess (Figure 5).

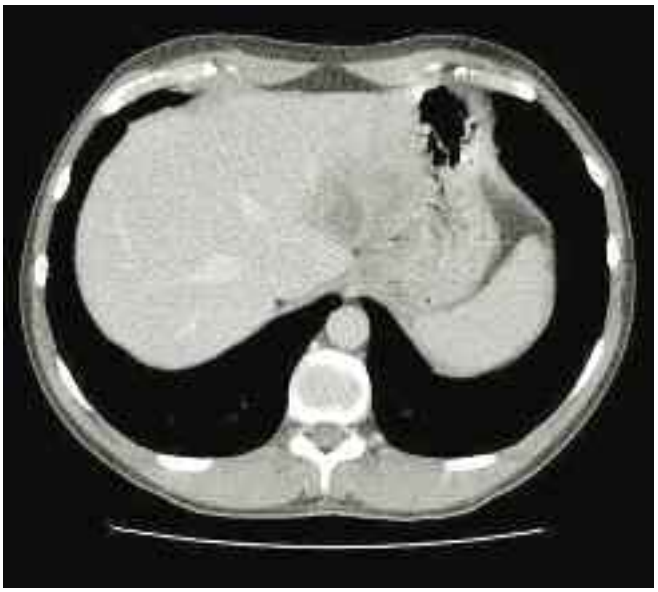

Figure 5. Evolving abscess in left lobe of liver.

c. This liver abscess could be either amoebic or bacterial (pyogenic). Blood cultures and stool microscopy for ova, cysts and parasites were negative, but amoebic serology was strongly positive. Hence a diagnosis of amoebic liver abscess was made and the patient was treated with metronidazole and diloxanide, which led to a rapid and complete recovery. Only 10-15% of amoebic liver abscesses occur in the left lobe and these are less likely to present with typical clinical features and can rupture into the peritoneal, pleural or pericardial spaces. Amoebic serology has >95% sensitivity for detecting amoebic liver abscesses, but specificity is lower following recent intestinal amoebiasis and in endemic areas. Serology remains the best way to distinguish amoebic from pyogenic liver abscesses. There is no proven benefit from aspiration of uncomplicated amoebic liver abscesses [2].

Answers for Case 3

a. Viral hepatitis is most likely, but the possibility of a haematological malignancy or even primary HIV infection should also be considered. Although the liver transaminases are raised, these are typically > 1 000 U/l in acute hepatitis A, B or E. The sum of the leukocyte subsets is significantly lower than the total WCC, suggesting that there are abnormal leukocytes in circulation.

b. Serology for hepatitis E virus (HEV), Epstein-Barr virus (EBV), cytomegalovirus (CMV) and HIV should be performed along with a blood film to look for atypical lymphocytes or blast cells.

c. Serology for HEV, CMV and HIV was negative, but there was serological evidence of acute EBV infection and atypical lymphocytes were also seen on the blood film. A diagnosis of EBV hepatitis was made and the patient revealed that his young son had recently had a non-specific febrile illness, which may have been the source. The patient was allowed home with monitoring of his LFTs and advised to avoid contact sports and arduous training for at least 3 and preferably 7 weeks due to the risk of splenic rupture [3]. He was also advised to regain full fitness with a gradual training programme to avoid a post-viral fatigue syndrome.

Answers for Case 4

a. This patient's wide range of symptoms is quite non-specific and could lead to a very wide differential diagnosis. However, the combination of fever, arthralgia (often reported as myalgia) and a rash would yield a much narrower

differential diagnostic of infectious and autoimmune disorders. This patient also has a relative bradycardia (considering his fever of 38.2 °C), which is said to occur in typhoid fever, leptospirosis, rickettsia infections (eg. typhus and spotted fevers) and arbovirus infections (eg. dengue and sandfly fevers) [4,5]. However, this sign is probably unreliable in extremely fit military personnel, who may not exhibit a tachycardia even when they have severe sepsis. A febrile illness with leukopenia and thrombocytopenia could be due to a wide range of infections (eg. malaria, visceral leishmaniasis, disseminated TB, brucellosis, rickettsiae, arboviruses, HIV or parvovirus), severe sepsis (with disseminated intravascular coagulation), autoimmune disorders and haematological malignancies. However, the patient's overall well-being and normal inflammatory markers (ESR and CRP) make non-viral infections, autoimmune disorders and haematological malignancies less likely.

b. Serology for arbovirus, HIV and parvovirus infections are the most obvious investigations to perform because the other possible diagnoses can largely be excluded by considering the combination of clinical features and laboratory results described.

c. Arbovirus serology tests showed evidence of acute dengue fever, which due to its short incubation period must have been acquired on his holiday in Thailand rather than any of his military deployments. Dengue fever typically presents with fever, arthralgia and rash. However, the rash occurs in only 50% of cases, is difficult to see in dark skin and rarely has the classic appearances of erythema with "islands of sparing" (Figure 6). The more severe manifestations of dengue haemorrhagic fever (DHF) and dengue shock syndrome (DSS) may develop later, but are very rare in people infected with dengue virus for the first time. Uncomplicated dengue fever requires symptomatic treatment only, but significant post-infection fatigue may occur. DHF and DSS have a 30% mortality if untreated, but this falls to <1% if appropriate resuscitation and supportive treatments are used. Chikungunya is a similar arbovirus infection (but does not cause haemorrhage or shock), which has recently re-emerged in countries bordering the Indian Ocean.

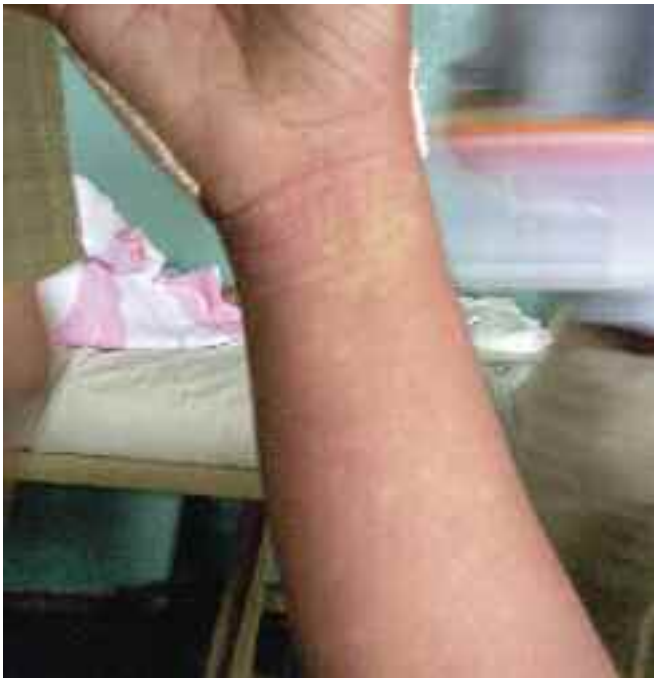

Figure 6. Classic rash of dengue fever.

Answers for Case 5

a. The "bruising" is actually erythema nodosum, which may be associated with certain infections (eg. Streptococci, Mycoplasma, TB), non-infectious disorders (eg. sarcoidosis, inflammatory bowel disease, SLE, haematological malignancies), pregnancy and a variety of drugs. However, up to 50% of cases are idiopathic.

b. Few of the further investigations required are possible in a field hospital environment, but a CXR showed bilateral hilar lymphadenopathy suggestive of sarcoidosis (Figure 6). The combination of fever, arthritis, erythema nodosum and bilateral hilar lymphadenopathy is a form of sarcoidosis sometimes referred to as Löfgren's syndrome and usually carries a good prognosis [6]. This patient was medically-evacuated to the UK where this diagnosis was confirmed.

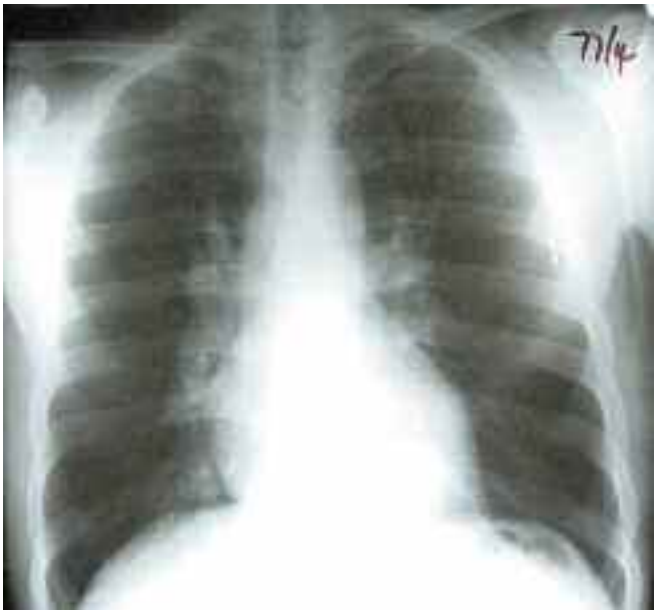

Figure 7. Bilateral hilar lymphadenopathy suggestive of sarcoidosis.

References

1. Garvin KW, Singh V. Case report: cutaneous myiasis caused by Dermatobia hominis, the human botfly. *Travel Med Infect Dis*. 2007; **5**: 199-201.
2. Chavez-Tapia NC, Hernandez-Calleros J, Tellez-Avila FI, Torre A, Uribe M. Image-guided percutaneous procedure plus metronidazole versus metronidazole alone for uncomplicated amoebic liver abscess. *Cochrane Database Syst Rev*. 2009; **1**: CD004886.
3. Putukian M, O'Connor FG, Stricker P *et al*. Mononucleosis and Athletic Participation: An Evidence-Based Subject Review. *Clin J Sport Med*. 2008; **18**: 309-15.
4. Lateef A, Fisher DA, Tambyah PA. Dengue and relative bradycardia. *Emerg Infect Dis*. 2007; **13**: 650-1
5. Wittesjö B, Björnham A, Eitrem R. Relative bradycardia in infectious diseases. *J Infect*. 1999; **39**: 246-7.
6. Grunewald J, Eklund A. Löfgren's syndrome: human leukocyte antigen strongly influences the disease course. *Am J Respir Crit Care Med*. 2009; **179**: 307-12.