Clinical imported fever cases

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Fever from West Africa

- January 2015, Liverpool UK
- Adult male referred by telephone call from Public Health England with fever after returning from Sierra Leone
- Doctor, was working in Ebola treatment centre
- Now has 48 hours of:
  - Fever, rigors
  - Myalgia, headache, arthralgia
- You are the doctor receiving the call

Question 1. What is the most important feature to ask about now?

1. Activity in Ebola centre
2. Dates of fever onset and last Ebola exposure
3. Presence of diarrhoea
4. Presence of haemorrhage or bruising
5. Use of malaria prophylaxis

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Question 2. What is the most likely diagnosis?

1. Dengue
2. Ebola virus disease
3. Enteric fever
4. Malaria
5. Respiratory infection

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Detail on arrival

- Worked in Ebola treatment centre for 10 weeks
- No breaches of PPE (Personal protective equipment)
- Slept in air conditioned hotel
- Doxycycline malaria prophylaxis until return (missed 2 doses)
- Symptom onset 24 days after leaving Africa

Findings

- Temperature 38°C
- BP etc normal, no other abnormal findings

- Haemoglobin 134 g/L (13.4 g/dL)
- Total white cell 5.8 x 10^9/L
- Lymphocytes 0.3 x 10^9/L
- Platelets 95 x 10^9/L

- Urea, electrolytes, liver function normal
- Chest x ray normal

Question 3. What is the most important next test?

1. Blood cultures
2. Clotting tests
3. Ebola virus tests
4. Malaria rapid diagnostic test
5. Malaria thin films

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Exclusion of viral haemorrhagic fever

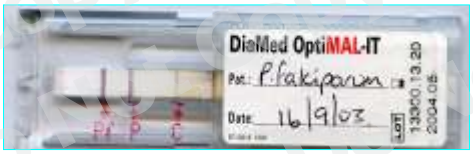
- Onset of symptoms more than 21 days after last possible exposure
- Therefore Ebola NOT likely in this patient (24 days)

Malaria RDTs

- Immunochromographic lateral flow assays for
  - *P. falciparum* Histidine Rich Protein 2
  - Or Parasite lactate dehydrogenase or aldolase
- Routinely used together with thin films in UK hospitals

Lab diagnosis of malaria

- Antigen detection Sensitivity a bit less than expert thick films



HRP2, LDH or aldolase

- PCR Mainly research ?

Malaria RDTs

- Immunochromographic lateral flow assays for
  - *P. falciparum* Histidine Rich Protein 2
  - Or Parasite lactate dehydrogenase or aldolase
- Routinely used together with thin films in UK hospitals
- Sensitivity for *P. falciparum* about the same as good thick films
- Fairly good for *P. vivax*
- Often miss *P. ovale* and *P. malariae*

Progress

- Rigors and fever to 40°C over next 48 hours
- Malaria thin films x 3 sets and RDT negative
- Blood cultures negative at 48 hours
- Multiplex respiratory PCR on pharyngeal swab positive for rhinovirus RNA
- Empirical treatment with ceftriaxone no effect

Question 4. What will you do now?

1. Continue ceftriaxone for 3 more days
2. Malaria thick films
3. Phone a friend in desperation
4. Relent and do Ebola tests
5. Treat for malaria

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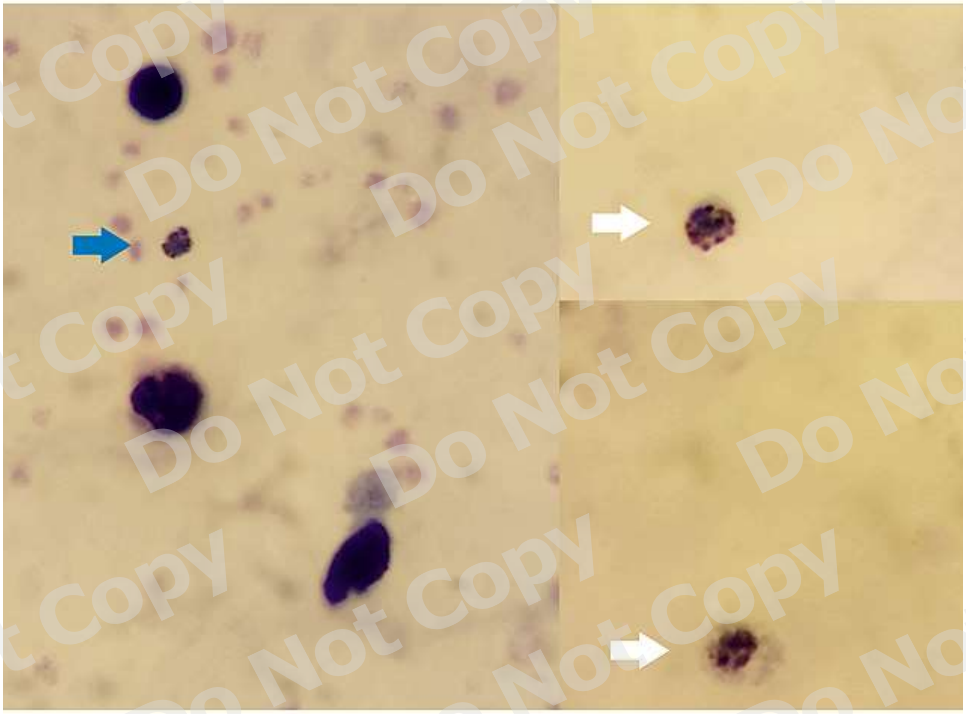
The outcome

Scanty malaria parasites seen on thick films at LSTM and pan malaria PCR (RIPL) positive



Question 5. What species of malaria do you think this is?

1. *P. falciparum*
2. *P. knowlesi*
3. *P. malariae*
4. *P. ovale*
5. *P. vivax*

Question 5. What species of malaria do you think this is?

1. *P. falciparum*
2. *P. knowlesi*
3. *P. malariae*
4. *P. ovale*
5. *P. vivax*

Reference laboratory (HTD London)

- Species specific PCR positive for *P. malariae*

Fever from Africa

- From West Africa or sub Saharan Africa
  - 60% likelihood of *P. falciparum* if gets to hospital
  - 95% likely if thrombocytopenia also present
  - Other species *P. ovale* W Africa, *P. vivax* elsewhere followed by *P. malariae* everywhere
- Next most common are respiratory and enteric infections
- Consider exotica such as rickettsial infections (tick typhus), dengue etc

GeoSentinel fever study n=6957

	Fever	Mal	DEN	No diag	Resp	Diarrh
Oceania	51	59	6	12	10	4
SS Africa	41	42	1	19	10	10
SE Asia	33	7	18	22	17	17
SC Asia	27	7	9	20	14	22
N Asia	24	1	0	26	39	11
N Africa	22	5	1	13	13	38
All		21	6		14	15

Figures are % of travellers returning from each region

Wilson M *et al. CID* 2007;44:1560-8

Common malarial misconceptions

- Fever pattern must be regular
- Splenomegaly must be present
- Chemoprophylaxis is 100% effective
- Blood films will be positive (NB effect of prophylaxis reducing parasitaemia)
- RDTs detect all species of malaria

Q6. How would you treat him (for *P. malariae)?*

1. Artesunate IV
2. Artemether/lumefantrine (ACT) oral
3. Atovaquone/proguanil
4. Choloroquine alone
5. Chloroquine and primaquine

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Treatment of non falciparum malaria

- Chloroquine for all 4 species
- Even in regions where there is resistant vivax
- Alternative is ACT
- ACT probably better for *P. knowlesi*
- Artesunate for severe *P. knowlesi* (often mistaken for *P. falciparum*)
- Add primaquine for *P. ovale* and *P. vivax* hypnozoites, best started at same time as chloroquine

Viral haemorrhagic fevers

- Even during major outbreak, malaria is a much more likely diagnosis
- Initial evaluation includes
  - Precise travel history
  - With dates
  - Possible occupational and recreational exposures (omitted later in Ebola epidemic)
- Suspect cases isolated with limited tests according to national protocols

Beeching NJ et al. Travellers and viral haemorrhagic fevers – what are the risks? *Int J Antimicrobial Agents* 2010; 36(Suppl): S26-S39 http://www.ijaaonline.com/article/S0924-8579%2810%2900258-X/fulltext

Fletcher TE, et al. Ebola and other viral haemorrhagic fevers. *BMJ* 2014; 349: g5079 www.bmj.com/content/349/bmj.g5079

Recent Liverpool Ebola "cases"

- Nigeria — Influenza A
- Sierra Leone — Norovirus (UK acquired)
- Nigeria — Falciparum malaria
- Nigeria — Falciparum malaria
- Cameroon — Otitis media/health tourism
- Sierra Leone — Norovirus
- Sierra Leone — Respiratory infection
- Sierra Leone — Malariae malaria
- Sierra Leone — Falciparum malaria
- Sierra Leone — Campylobacter

- Nigeria – child — Influenza B

Summary of lessons

- Always take a travel history
- Fever from sub Saharan or West Africa is due to malaria until proved otherwise
- Interpret tests with variable sensitivity in light of this pre test probability
- Consider possibility of empirical treatment for malaria if patient severely ill
- PCR may have a role in diagnosis of malaria
- Viral haemorrhagic fevers are MUCH less common but need precise travel history to rule in/out on epidemiological grounds

CASE RECORDS of the MASSACHUSETTS GENERAL HOSPITAL

N Engl J Med 10 Sep 2015; 373:1060-7

Founded by Richard C. Cabot

***P. falciparum* malaria**

Case 28-2015: A 32-Year-Old Man with Fever, Headache, and Myalgias after Traveling from Liberia

Paul D. Biddinger, M.D., David C. Hooper, M.D., Erica S. Shenoy, M.D., Ph.D., Ednan K. Bajwa, M.D., M.P.H., Gregory K. Robbins, M.D., M.P.H., and John A. Branda, M.D.

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