Malaria

Epidemiology, diagnosis and risk of resurgence

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When patients are admitted we seldom know immediately what the diagnosis is.

We must decide:

- Which samples for analysis, isolation or not
- High risk patient based on travel history (West Africa)
- Treatment to be started before a clear diagnosis

We do this based on:

- History and physical examination
- Laboratory testing and RDTs (Rapid Diagnostic tests)
- Geography of travel and earlier life (migration)
**VIRAL HAEMORRHAGIC FEVERS RISK ASSESSMENT** (Version 3: 11.08.2014)

A) Does the patient have a fever (>38°C) or history of fever in past 24 hours AND has returned from (or is currently residing in) a VHF endemic country (http://www.hpa.org.uk/Topics/InfectiousDiseases/InfectionsAZ/ViralHaemorrhagicFever/VHFMaps/) within 21 days? OR

B) Does the patient have a fever (>38°C) or history of fever in past 24 hours AND has cared for / come into contact with body fluids of handled clinical specimens (blood, urine, faeces, tissues, laboratory cultures) from an individual or laboratory animal known or strongly suspected to have VHF?

- **NO to A AND B**
  - VHF Unlikely; manage locally

- **YES to A only**
  - Additional questions:
    - Has the patient travelled to any area where there is a current VHF outbreak? (http://www.promedmail.org/)
    - Has the patient lived or worked in basic rural conditions in an area where Lassa Fever is endemic? (http://www.hpa.org.uk/webu/HPAweb&HPAwebAutoListName/Page/119142150101)
    - Has the patient visited caves OR mines, or had contact with primates, antelopes or bats in a Marburg / Ebola endemic area? (http://www.hpa.org.uk/webu/HPAweb&HPAwebStandard/HPAweb_C/125511988573)
    - Has the patient travelled in an area where Crimean-Congo Haemorrhagic Fever is endemic? (http://www.hpa.org.uk/webu/HPAweb&HPAwebStandard/HPAweb_C/119573771894) AND sustained a tick bite* or crushed a tick with their bare hands OR had close involvement with animal slaughter?

- **YES to B**
  - **ADDITIONAL QUESTIONS:**
    - Has the patient worked in an area where Lassa Fever is endemic? (http://www.hpa.org.uk/webu/HPAweb&HPAwebAutoListName/Page/119142150101)
    - Has the patient travelled to any area where there is a current VHF outbreak? (http://www.promedmail.org/)
    - Has the patient lived or worked in basic rural conditions in an area where Lassa Fever is endemic? (http://www.hpa.org.uk/webu/HPAweb&HPAwebAutoListName/Page/119142150101)
    - Has the patient visited caves OR mines, or had contact with primates, antelopes or bats in a Marburg / Ebola endemic area? (http://www.hpa.org.uk/webu/HPAweb&HPAwebStandard/HPAweb_C/125511988573)
    - Has the patient travelled in an area where Crimean-Congo Haemorrhagic Fever is endemic? (http://www.hpa.org.uk/webu/HPAweb&HPAwebStandard/HPAweb_C/119573771894) AND sustained a tick bite* or crushed a tick with their bare hands OR had close involvement with animal slaughter?

**INFECTION CONTROL MEASURES**

**MINIMAL RISK**

- Standard precautions apply.
  - Hand hygiene, gloves, plastic apron.
  - Eye protection and fluid resistant surgical face mask and for splash inducing procedures.
  - Patients that have extensive bruising, active bleeding, uncontrolled diarrhoea, uncontrolled vomiting.
  - Hand hygiene, double gloves, fluid repellent disposable gown/suit, eye protection, FFP3 respirator.

**STAFF AT RISK**

- Hand hygiene, gloves, plastic apron, fluid repellent surgical face mask and for splash inducing procedures.
- Patients that have extensive bruising, active bleeding, uncontrolled diarrhoea, uncontrolled vomiting.
- Hand hygiene, double gloves, fluid repellent disposable gown/suit, eye protection, FFP3 respirator.

**STAFF AT HIGH RISK**

- Hand hygiene, double gloves, fluid repellent disposable gown or suit, plastic apron (over disposable gown/suit) eye protection, FFP3 respirator.

**HIGH POSSIBILITY OF VHF**

- **ISOLATE PATIENT IN A SIDE ROOM**
  - Urgent Malaria investigation
  - Full blood count, U&E, LFTs, clotting screen, CRP, glucose, blood cultures
  - Inform laboratory of possible VHF case (for specimen waste disposal purposes if confirmed)
  - Discuss with Infection Consultant (Infectious Disease/Microbiology/Virology).
  - Infection Consultant to arrange VHF screen with Imported Fever Service (0844 7788990)
  - Notify Local Health Protection Unit
  - Consider empiric antimicrobials

**CLINICAL QUESTION TO DETERMINE INFECTION CONTROL BEHAVIOUR AND PROTECT STAFF:** does the patient have extensive bruising or active bleeding?

- **YES**
  - Discuss with Infection Consultant (Infectious Disease/Microbiology/Virology).
  - Possibility of VHF; Infection Consultant to consider discussion of VHF screen with Imported Fever Service (0844 7788990)

- **NO**
  - Patient fit for outpatient management?
    - **YES**
      - Inform/update Local Health Protection Unit
      - Ensure patient contact details recorded
      - Patient self isolation
      - Follow up VHF screen result
      - Review daily
    - **NO**
      - Is the patient fit for outpatient management?
        - **YES**
          - VHF unlikely; manage locally
        - **NO**
          - Clinical concern OR continuing fever after 72 hours?
            - **YES**
              - Alternative diagnosis confirmed?
                - **YES**
                  - VHF unlikely; manage locally
                - **NO**
                  - VHF unlikely; manage locally
            - **NO**
              - Clinical concern OR continuing fever after 72 hours?
                - **YES**
                  - VHF unlikely; manage locally
                - **NO**
                  - Is the patient fit for outpatient management?
                    - **YES**
                      - Inform/update Local Health Protection Unit
                      - Ensure patient contact details recorded
                      - Patient self isolation
                      - Follow up VHF screen result
                      - Review daily
                    - **NO**
                      - Manage locally

- **CONFIRMED VHF**
  - Contact High Level Isolation Unit for transfer (020 7794 0500: Royal Free)
  - Launch full public health actions, including categorisation and management of contacts
  - Inform lab if other lab tests are needed

Please note this algorithm is a guide designed to aid early diagnosis of VHF cases.
You have now excluded a haemorrhagic fever

What can cause fever and Disseminated Intervascular Coagulation?

- Septicemia – both gr+ and gr-
- Leptospirosis
- Malaria
- Dengue, Yellow fever
- CCHF, Alkhurma Hemorrhagic Fever

Biochemistry (Hb, WBC, Thrc, CRP, liver- and kidney parameters, BS, Malaria microscopy or rapid test, DIC parameters), blood culture

Blood pressure, pulse, resp. rate or O₂ saturation, p-lactate

Treatment?

Antibiotics? Malaria drugs?
Case fatality rate’s

Overall *P.falciparum* (1977-86) 1.3

Range in Europe 0.5 - 5.8

Switzerland 1988-2002 2.2


A cluster of 56 patients returning from Gambia with falciparum malaria has been noted in several countries of the European Union since September this year. TropNetEurop, the European Network on Imported Infectious Disease Surveillance, collected and reported the cases. Lack of awareness and, consequently, of prophylactic measures against malaria were apparent in the majority of patients.

**The Netherlands**

In the Netherlands, 10 Dutch tourists were reported with falciparum malaria after returning from Gambia between 21 September and 26 November 2008. The median age was 48 years (range 43-62), six patients were female. Three cases were related (travel companions). The median duration of stay was nine days (range 7-68). Seven travellers did not use malaria chemoprophylaxis, two used homeopathic drugs (chininum arsenicumum D8) and one tourist stopped atovaquone/proguanil prematurely. The median shortest incubation period was five days (range 0-18). The median interval between the first day of illness and the date of diagnosis was five days (range 0-17). Seven patients were admitted to hospital for treatment. Two patients, aged 45 and 49, died. Both patients had not used chemoprophylaxis. The time to diagnosis was 17 and six days, respectively [3].

3 patients died = 5.3% (3/56)
Figure 2: Global distribution of infection with *Plasmodium falciparum* malaria
Reproduced from Hay and Snow, and licensed to the Malaria Atlas Project (http://www.map.ox.ac.uk). PfAPI = *P. falciparum* annual parasite incidence per 1000 people per year. PfPR = *P. falciparum* parasite rate age-standardised to 2–10 years.
Pre control
Malaria, the present challenge

16th April 2014
600 imported cases in 2013

Several cases in the International City

2788 cases diagnosed since 2011

26th June 2012
2731 imported cases in 2011

12 April 2014
1440 cases reported in 2013. 11 autochthonous cases
Oman interrupted malaria transmission in 2004 and maintained it until September 2007, when a focus of local transmission (with 4 cases) was detected in Dakhiliya governorate. Secondary cases occurred in North Sharqiya governorate in 2010, North Sharqiya and Dakhiliya in 2011, and North and South Sharqiya and North Batinah in 2012. The number of imported cases started to show a decrease from 2029 in 2012 to 1440 cases in 2013. Of the total 1451 cases recorded in 2013, the majority (99.24 percent) were internationally imported except for 11 secondary cases. 


Immigrants from the Asian subcontinent being asymptomatic gametocyte carriers starting a limited local transmission. Genetic fingerprinting needed to determine if it is a single or multiple introduction.
*P. falciparum* are imported from Africa and *P. vivax* from Asia

<table>
<thead>
<tr>
<th>Region of acquisition [1]</th>
<th><em>P. falciparum</em></th>
<th><em>P. vivax</em></th>
<th>P. ovale</th>
<th>P. malariae</th>
<th>Mixed</th>
<th>2013 total</th>
<th>2012 total</th>
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<tr>
<td>Western Africa</td>
<td>826</td>
<td>1</td>
<td>49</td>
<td>21</td>
<td>9</td>
<td>906</td>
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<td>1</td>
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<td>-</td>
<td>-</td>
<td>1</td>
<td>1</td>
<td>1</td>
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<tr>
<td>Eastern Asia</td>
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<td>-</td>
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<td>1</td>
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<tr>
<td>South America</td>
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<td>-</td>
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<td>-</td>
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<tr>
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<td>6</td>
<td>1</td>
<td>2</td>
<td>109</td>
<td>147</td>
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<tr>
<td><strong>Total</strong></td>
<td><strong>1192</strong></td>
<td><strong>179</strong></td>
<td><strong>78</strong></td>
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<td><strong>13</strong></td>
<td><strong>1501</strong></td>
<td><strong>1378</strong></td>
</tr>
</tbody>
</table>

Malaria in Europe

A question of climate change?

Finland 1937 – 45

Germany 1945 – 49

Poland 1945 – 56

The Netherlands 1946 – 48

Armenia, Azerbaijan 1993 – 2002

Greece 2011 – 2013
COMMUNICABLE DISEASE THREATS REPORT
CDTR Week 37, 9-15 September 2012
All users
This weekly bulletin provides updates on threats monitored by ECDC.
I. Executive summary
EU Threats
Malaria - Greece - 2012
Opening date: 31 May 2012 Latest update: 7 September 2012
Since June 2012, eight autochthonous cases of malaria, caused by *Plasmodium vivax* infection, have been reported from Greece. Local control measures have been implemented in accordance with national guidelines.

Update of the week
No additional autochthonous cases were reported since the last update.

Three *P. vivax* cases reported in 2013, none in 2014

In the outbreak over?
Long latency *P. vivax* (*P. vivax hibernans*)

*P. vivax* - different phenotypes


**P. vivax haplotypes**

Temperate zone *P. vivax*

Figure 2: A haplotype network based on *P. vivax* mt genome sequences. Each circle represents a haplotype with size of the circle equaling to the frequency of the haplotype in the samples. Lines separating haplotypes represent mutational steps. Each color shows the countries of origin of the samples.

Diagnosis of malaria
Malaria: thick blood films

1. Collect blood from a finger prick.

2. Apply the blood to the slide.

3. Allow the blood to dry.

4. Dry the slide, and it can be sent by mail.

Dry the slide, and it can be send by mail.
Plasmodium falciparum – thin blood films

Ring forms

Ring forms

Schizont - early

Schizont - late

Schizont - burst

Schizont - burst

Gametocyte

Gametocytes
Centers managing patients with malaria must be able to provide round the clock malaria microscopy of thick and thin blood films and parasite density calculations.

Rapid tests may be false negative in cases with:

- **very high** *P. falciparum* density ?? (Gillet et al. Malaria J 2009; 8:271)
  (HRP2 deletion in parts of South America)
- **Variant P. ovale** (Tordrup et al. Malaria J 2011;10:15)
- **P. knowlesi**

HRP2 based tests will be negative sensitivity variable with other tests

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**Malaria Rapid Diagnostic Test Performance – Results of WHO product testing of malaria RDTs: Round 3 (2010-2011)**

The evaluation programme is co-sponsored by the Foundation for Innovative New Diagnostics (FIND), the Special Programme for Research and Training in Tropical Diseases (TDR) and the WHO Global Malaria Programme (GMP). Testing is performed at the US Centers for Disease Control and Prevention (CDC)

Use a rapid test which include pan Plasmodial antigen ie. LDH or Aldolase
Which method should we use?

Detection levels of different diagnostic methods:

<table>
<thead>
<tr>
<th>Method</th>
<th>Level of Parasites per mm$^3$</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rapid tests</td>
<td>200</td>
<td>WHO 2011</td>
</tr>
<tr>
<td>PCR</td>
<td>0.5</td>
<td>Gama BE et al. Exp Parasitol. 2007 Mar 2; [Epub]</td>
</tr>
</tbody>
</table>
The development of immunity to malaria

Figure 1. Age-specific parasite rates and positive parasite densities for asexual parasites of *Plasmodium falciparum* and *Plasmodium malariae*. Left axis shows geometric mean positive parasite density as parasites per microliter; right axis shows parasite rate. Category axis shows age groups in days (to age 182 days) and in years. Pregnant women were excluded.

Semi-immune
Conclusion

Previous malaria endemic areas still have the mosquitoes and thus have transmission potential

Asymptomatic gametocyte carriers from endemic areas constitute a constant risk in areas with transmission potential

Diagnosis of asymptomatic carriers is a challenge because of the low parasite density in semi-immunes
Thank you questions?

Thank you very much.

- Thank you very much -