The Imported Fever Service

Dr Nick Beeching
Federation of Infection Societies
Birmingham 13 Nov 2013

Drs Jon Lambourne, Alex Aiken et al
ID-Microbiology Specialist Trainees
Public Health England
Rare and Imported Pathogens Lab
Salisbury, England
Disclosures

None relevant
Overview

Origins & Aims of the Service
How it works
Results so far
Service utility & user satisfaction
Conclusions & future developments
29 year old female, no PMH
- Unwell with fever, rigors & myalgia, 3 days after return from N. Malaysia
- 2 days later admitted hospital with breathlessness & pleuritic chest pain
- 24-hours into admission has a large pulmonary haemorrhage -> ITU

Investigations:
Anaemia (12.1g/l), lymphopenia (0.4 x10⁹/L) & thrombocytopenia (52 x10⁹/L)
Coagulation profile, renal function & liver function tests all normal
A quick case...
Overview

Origins & Aims of the Service

How it works

Results so far

Service utility & user satisfaction

Conclusions & future developments
Fever in the returned traveller

- Frequent problem
- Wide array of causes
  - Difficult to differentiate on clinical grounds
  - Lab diagnosis varies from ‘routine’ to ‘exotic’
  - Guidelines exist for UK management
  - Diagnostic delay associated with worse outcome

1 Leder K et al. Ann Intern Med 2013;158:456-68
3 Johnston V et al,  JOI 2009; 59: 1-18
4 Checkley A et al,  BMJ 2012;344:e2116
Diagnosing ‘exotics’ pre-Fever Service

Patient with fever of unknown origin

Form A

Lab A

Time = days, weeks

Result

Form B

Lab B

Lab C

Lab D

Wrong lab

No Result
Shortcomings of this model

• Exemplified by case of Lassa Fever, imported into UK in 2009\(^1\)
  • >14-day delay from presentation to diagnosis
  • Delay in ribavirin, may have contributed to patient demise
  • Substantial public health implications
    – Including 328 healthcare worker contacts

• Why this delay?
  • Lack of awareness of possibility of VHF
  • Lack of awareness of testing facilities for ‘exotic’ pathogens

Need for an integrated service to identify and manage ‘exotic’ infections in travellers returning to the UK with undiagnosed fever

\(^1\)Kitching A et al. Euro Surveill. 2009;14(6):pii=19117
Imported Fever Service model

Patient with fever of unknown origin

Clinical Advice hotline
Advice on:
• Samples required
• Interim patient management
• Interim infection control measures

Single web form
Sample(s)
Lab
1 day
Result + Interpretation
Public Health England

Imported Fever Service model

Patient with fever of unknown origin

Clinical Advice hotline

Advice on:
• Samples required
• Interim patient management
• Interim infection control measures

Single web form

Sample (s)

Lab

1 day

Result + Interpretation

‘Live’ since June 2012
Main roles of IFS

1. **Clinical & infection control advice**
   - Single point of contact, 24/7
   - Consider differential diagnoses & empiric Rx
   - Accurate VHF-risk assessment

2. **Diagnostic service**
   - Rapid turnaround with simplified logistics
   - Explanation of results

3. **Support Public Health responses**

4. **Research & Development**
   - e.g. new diagnostics
Overview

Origins & Aims of the Service

How it works

Results so far

Service utility & user satisfaction

Conclusions & future developments
Local team call Fever Service

Answered by Trainee or Consultant (24/7, 365)

Case details taken

Advice given: clinical, infection control, diagnostics

Diagnostics • ‘Panel testing’

Clinical • Case discussed within FS clinical network

Local team called with results & clinical feedback

Imported Fever Service +44 844 77 88 990
RIPL ‘Geographic panel’ testing

Patient travel history determines which tests performed:
- 10 world regions  =>  ‘Panel’ of tests for each region
e.g. ‘South-East Asia screen’

* Dengue, West Nile, JE, Tick-borne, Chikungunya, Rickettsia, Orientia, Leptospirosis *

**Costs** (excluding shipping)

- VHF screen:  free
- Single serology/IF: £58
- Single PCR: £78
- Panel: £128
## Rare & Imported Pathogens Lab assays

**2-3 Working Days**

<table>
<thead>
<tr>
<th>PCR assays</th>
<th>Dengue virus</th>
</tr>
</thead>
<tbody>
<tr>
<td>Malaria</td>
<td>West Nile virus</td>
</tr>
<tr>
<td>CCHF</td>
<td>Japanese encephalitis virus</td>
</tr>
<tr>
<td>Lassa</td>
<td>TBE virus</td>
</tr>
<tr>
<td>Marburg</td>
<td>Yellow fever virus</td>
</tr>
<tr>
<td>Ebola</td>
<td>Kunjin virus</td>
</tr>
<tr>
<td>Dengue</td>
<td>Murray Valley virus</td>
</tr>
<tr>
<td>Rift Valley fever virus</td>
<td>St Louis Encephalitis virus</td>
</tr>
<tr>
<td>Hantaviruses</td>
<td>Chikungunya virus</td>
</tr>
<tr>
<td>La Crosse virus</td>
<td>Ross River virus</td>
</tr>
<tr>
<td>Sandfly fever viruses</td>
<td>Mayaro virus</td>
</tr>
<tr>
<td>LCMV</td>
<td>Equine Encephalitis viruses</td>
</tr>
<tr>
<td></td>
<td>Sindbis virus</td>
</tr>
<tr>
<td></td>
<td>Hendra &amp; Nipah virus</td>
</tr>
</tbody>
</table>

### Urgent on-call

- *PCR assays*
  - Malaria
  - CCHF
  - Lassa
  - Marburg
  - Ebola
  - Dengue

### Parasitology

- HTD
Overview

Origins & Aims of the Service
How it works
Results so far
Service utility & user satisfaction
Conclusions & future developments
Number of referrals: June ‘12 – July ‘13

Total referrals = 240
From 113 centres
# Travel destinations & presenting complaints

<table>
<thead>
<tr>
<th>Region of travel</th>
<th>Total</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Africa</td>
<td>94</td>
<td>39.2</td>
</tr>
<tr>
<td>Asia</td>
<td>57</td>
<td>23.8</td>
</tr>
<tr>
<td>Europe</td>
<td>31</td>
<td>12.9</td>
</tr>
<tr>
<td>UK</td>
<td>29</td>
<td>12.1</td>
</tr>
<tr>
<td>North America</td>
<td>13</td>
<td>5.4</td>
</tr>
<tr>
<td>South America</td>
<td>10</td>
<td>4.2</td>
</tr>
<tr>
<td>Australia / South Pacific</td>
<td>6</td>
<td>2.5</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Complaint or lab problem</th>
<th>Totals</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Undifferentiated fever</td>
<td>77</td>
<td>29.2</td>
</tr>
<tr>
<td>Neurological</td>
<td>55</td>
<td>20.8</td>
</tr>
<tr>
<td>Rash / Skin</td>
<td>28</td>
<td>10.6</td>
</tr>
<tr>
<td>Respiratory</td>
<td>25</td>
<td>9.5</td>
</tr>
<tr>
<td>Sepsis</td>
<td>24</td>
<td>9.1</td>
</tr>
<tr>
<td>Haematological</td>
<td>14</td>
<td>5.3</td>
</tr>
<tr>
<td>Gastrointestinal</td>
<td>11</td>
<td>4.2</td>
</tr>
<tr>
<td>Musculoskeletal</td>
<td>9</td>
<td>3.4</td>
</tr>
<tr>
<td>Renal impairment</td>
<td>7</td>
<td>2.7</td>
</tr>
<tr>
<td>Hepatitis</td>
<td>7</td>
<td>2.7</td>
</tr>
<tr>
<td>Cardiovascular</td>
<td>3</td>
<td>1.1</td>
</tr>
<tr>
<td>Other</td>
<td>2</td>
<td>0.8</td>
</tr>
</tbody>
</table>
## Diagnoses following Fever Service referral

<table>
<thead>
<tr>
<th>TOTAL CASES</th>
<th>240</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cases with diagnosis</td>
<td>147 (61.2%)</td>
</tr>
<tr>
<td>Diagnoses made via FS referral</td>
<td>64 (26.7%)</td>
</tr>
</tbody>
</table>
Some diagnoses reached after discussion

Cutaneous syphilis
Neurosyphilis
Atypical haemolytic uraemic syndrome
Severe haemolysis
Haemophagocytic syndrome

NB Many difficult neurology cases
Overview

Origins & Aims of the Service

How it works

Results so far

Service utility & user satisfaction

Conclusions & future developments
User survey (n=108)

- 88% are satisfied with staff helpfulness
- 90% satisfied with the quality of advice given
- 100% satisfied with availability
- 85% believe 24-hour access is important
- 71% satisfied with turn-around time
Reasons for contacting the service

- Clinical advice
- Diagnostic advice
- Infection control advice
- Results interpretation
- Public health advice
- Logistics e.g. what sample, ...
- Other (please specify)
**Reported benefits of contacting the service**

- Confirmation of suspected diagnosis
- Diagnosis of pathogen or condition...
- Discharge from hospital
- Infection control precautions
- Antimicrobial therapy
- Contact with public health...
- Reassurance of staff, patients or...
- Interpretation of test...
- Knowledge & education
Overview

Origins & Aims of the Service

How it works

Results so far

Service utility & user satisfaction

Conclusions & future developments
A quick case...
A quick case…

Diagnostic timeline

17:30 case discussed with Fever Service
18:00 next day samples arrive in RIPL & ‘South East Asia panel’ run
00:30 results obtained & communicated to clinical team

PCR for pathogenic leptospira species positive on EDTA, BAL & urine

Diagnosis

Leptospirosis-associated Severe Pulmonary Haemorrhagic Syndrome

c/o Kate Adams/Charlotte Hall Hull RI
A quick case…

Progress

Antibiotic therapy rationalised to benzylpenicillin
- Day 4: off oscillator
- Day 9: successful extubation
- Day 10: transferred to ward
- Day 13: discharged

Learning points for the Fever Service & local team
- Significant pulmonary complications due to leptospirosis can occur without hepatic or renal compromise\(^1,2\)
- Benefit of ‘Geographic panel’ testing approach

Aims ➔ Benefits of the Fever Service

1. Clinical & infection control advice
   Single point of contact, 24/7
   Consider differential diagnoses & empiric Rx
   Accurate VHF-risk assessment

2. Diagnostic service
   Rapid turnaround with simplified logistics
   Explanation of results

3. Support Public Health responses

4. Research & Development
   e.g. new diagnostics
Weekly Tele-Conference

Friday mornings 1130 – 1215 ish

All Core IFS centres plus others

Recently encouraged presentation from & involvement of referring centres

Chaired by IFS StR, including summaries before & after

Recorded and transcribed – possible educational podcast

Care regarding confidentiality issues

Educational resource in real time, and bank of teaching cases

Considering wider availability
Recent case - Liverpool

69 year old Thai woman
Resident UK for years
Diabetic

Visited semi urban area near Bangkok for 10 days returning 28 Oct 13

Admitted 2 days later
Short flu like illness
Hypotensive
Acidotic
Severe pneumonia
Recent case - Liverpool

Imported Fever Service
Diagnosis?

1. Avian flu
2. Leptospirosis
3. Melioidosis
4. MERS-CoV
5. Swine flu
6. Other
Diagnosis?

1. Avian flu
2. Leptospirosis
3. Melioidosis
4. MERS-CoV
5. Swine flu

6. Other: Parainfluenza and Staph aureus bacteraemia
Case from Americas

32 year old Male

Travel in S America June-Aug 2013, returned early Sep 13

Peruvian amazon; June: Peru mountains; July-Aug: Bolivia, Chile, Argentina, Brazil.

On holiday, adventurous travel, rivers, jungle, mountains, no close animal contact

Mid-Aug 2013

Inflamed abscess developed on R forehead/ ?insect bite.
Remained for 8 weeks, no change
No response from 1 week coamoxiclav
No fever, not systemically unwell
Diagnosis?

1. Bartonellosis
2. Chagas disease
3. Leishmaniasis
4. Myiasis
5. Pyogenic infection
6. Other
Diagnosis?

1. Bartonellosis
2. Chagas disease
3. Leishmaniasis (PCR)
4. Myiasis
5. Pyogenic infection
6. Other
Conclusions

- The Fever Service is the first service of its kind in the world
- The FS model improves the capacity to diagnose fever in returned travellers in a clinically relevant timeframe
- Diagnosis facilitates patient care, public health response and knowledge
- The FS model could be implemented in other countries
Imported Fever Service

A national specialist service for acute imported fever diagnosis providing:
- Round-the-clock on-call expert clinical and microbiological advice to support patient management, infection control and public health interventions, from referral to delivery and interpretation of final results.
- A 24-hour on-call diagnostic service for viral haemorrhagic fevers.
- Next working day diagnostic service for a range of acute imported fevers of infectious origin.

**Referrals to the Fever Service**
- Patient with fever and recent history of foreign travel
- Discuss with the local consultant microbiologist, virologist or infectious diseases physician and perform local tests as required
- Call Fever Service telephone number with required patient information
- Obtain advice from on-call Fever Service specialist to support initial patient management, infection control and public health interventions required
- Send samples to local lab with:
  - Own referral form clearly citing "Fever Service"
  - The Fever Service Supplementary Information Sheet* where possible, to provide extra clinical information
- From the local lab send relevant samples to HPA Porton with:
  - P1 HPA-RIPE laboratory request form*, clearly citing "Fever Service"
  - The Fever Service Supplementary Information Sheet* where possible, to provide extra clinical information
- Obtain same day/next working day results from Fever Service lab with appropriate clinical advice

**Information required for contacting Fever Services**
- Contact number and details of the referring doctor
- Patient details (name, date of birth, address, current location)
- Clinical signs and symptoms (including onset of fever)
- Full travel history (countries and areas visited, dates of travel, activities undertaken, potential exposures, vaccination, chemoprophylaxis)
- Other relevant risk factors
- Relevant past medical history
- Available test results (blood tests, microbiology, radiology)
- Current clinical management (antimicrobials, intensive care support)

Fever Service telephone number:
0844 7788990

Only call this number following discussion with local consultant microbiologist, virologist or infectious disease physician.
**Referrals to the Fever Service**

- Patient with fever and recent history of foreign travel
- Discuss with the local consultant microbiologist, virologist or infectious diseases physician and perform local tests as required
- Call Fever Service telephone number with required patient information
- Obtain advice from on-call Fever Service specialist to support initial patient management, infection control and public health interventions required
- Send samples to local lab with:
  - Own referral form clearly citing "Fever Service"
  - The Fever Service Supplementary Information Sheet* where possible, to provide extra clinical information
- From the local lab send relevant samples to HPA Porton with:
  - P1 HPA-RIPL laboratory request form*, clearly citing "Fever Service"
  - The Fever Service Supplementary Information Sheet* where possible, to provide extra clinical information
- Obtain same day/next working day results from Fever Service lab with appropriate clinical advice

**Information required for contacting Fever Service:**

- Contact number and details of the referring doctor
- Patient details (name, date of birth, address, current location)
- Clinical signs and symptoms (including onset of fever)
- Full travel history (countries and areas visited, dates of travel, activities undertaken, potential exposures, vaccination, chemoprophylaxis)
- Other relevant risk factors
- Relevant past medical history
- Available test results (blood tests, microbiology, radiology)
- Current clinical management (antimicrobials, intensive care support)
Access

Imported Fever Service

About 3,630,000 results (0.27 seconds)

Ad related to imported fever service  
Lupus - what's that? - hibbslupustrust.org
www.hibbslupustrust.org/
Discover more about lupus symptoms, causes, diagnosis & treatment.
The Hibbs Lupus Trust has 327 followers on Google+

HPA - Imported Fever Service
www.hpa.org.uk › ... › Rare and Imported Pathogens Laboratory (RIPL)
21 Aug 2012 - A specialist service for the diagnosis of acute fevers due to travel-related infections.

HPA - Rare and Imported Pathogens Laboratory (RIPL)
www.hpa.org.uk › ... › Laboratories and Reference Facilities
A key programme is the Imported Fever Service, a joint venture between RIPD and the Hospital for Tropical Diseases (part of UCLH) and the Royal Liverpool ...
You've visited this page 3 times. Last visit: 05/08/13

[PDF] Imported Fever Service enquiries process
www.hpa.org.uk/webc/HPAwebFile/HPAweb_C/1317135713895
Rare and Imported Pathogens Laboratory (RIPL)

The Rare and Imported Pathogens Department (RIPD), HPA Microbiology Services is located at Porton Down Salisbury and operates the Rare and Imported Pathogens Laboratory (RIPL), formerly known as the Special Pathogens Reference Unit (SPRU).

RIPD has 23 staff including two medical consultant microbiologists, a full-time consultant infectious disease physician, a part-time consultant virologist, a dedicated SpR on rotation from University College Hospital, London (UCLH), a part-time clinical scientist and a post-doctoral trainee clinical scientist covering diagnostic work and medical advice for the NHS and other units nationally and internationally. Three dedicated post-doctoral scientists lead specialist research programmes covering diagnostics, vaccine studies ad biosafety. Operational management and a dedicated diagnostic development unit are provided by associated units.

A key programme is the Imported Fever Service, a joint venture between RIPD and the Hospital for Tropical Diseases (part of UCLH) and the Royal Liverpool Hospital’s Tropical and Infectious Diseases Unit. The department also provides strategic scientific advice and programme support to the Agency and beyond on a wide range of research topics, from vaccine design and development through evaluation of therapeutics to environmental spread of organisms and has three post-doctoral scientists covering this area. Many of the junior staff are studying for PhD or Masters degrees.
Team Fever Service

Rare & Imported Pathogens lab
Tim Brooks, Malur Sudhanva
Surabhi Taori, Carlos Varon,
Amanda Semper, Jane Osborne
Emma Aarons, Andrew Simpson,
Matthew Dryden
& all the lab staff
Ex-Fever Service Trainees
Cathy Roberts, Behzad Nadjm
Katherine Russell, Alex Aiken
Jon Lambourne, Paulo Hearn (current)

Liverpool
Nick Beeching
Alastair Miller

UCLH & HTD
Peter Chiodini et al
Nan Shetty

Manchester
Ken Mutton
Ed Kaczmarski

amanda.semper@phe.gov.uk