Risks and Risk assessment in Travel Medicine

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Travel Clinic
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Outline

- Basis of risk assessment
- Evidence for risk assessment
- Epidemiology of risks for travellers
  - Hepatitis A, Typhoid, Yellow fever
- Deaths in travellers
- Cases: managing risk in running a clinic
>95% of travel associated illness is not vaccine preventable
The Risk Assessment

- The assessment needs to reflect the health risks and not the interventions available
- Prioritise risks and select order of discussion
  - Common, treatable/avoidable, potentially fatal
- The assessment needs to be tailored to the individuals personal risk values or threshold
- Risk based on **best evidence** not perception or intuition
### How we communicate risk terminology often used

<table>
<thead>
<tr>
<th>High risk</th>
<th>Risk everywhere</th>
</tr>
</thead>
<tbody>
<tr>
<td>Risk variable</td>
<td>Risk varies</td>
</tr>
<tr>
<td>Risk low</td>
<td>No known risk</td>
</tr>
<tr>
<td>Risk very low</td>
<td>Continuous</td>
</tr>
<tr>
<td>Higher risk</td>
<td>Frequent</td>
</tr>
<tr>
<td>Increased risk</td>
<td>Infrequent</td>
</tr>
<tr>
<td>Potential risk</td>
<td>Rare</td>
</tr>
</tbody>
</table>
MedRA system; organ class and frequency category

Frequency categories are defined using the following convention:

- Very common (≥1/10)
- Common (≥1/100, <1/10)
- Uncommon (≥1/1,000, <1/100)
- Rare (≥1/10,000, <1/1,000)
- Very rare (<1/10,000)
- Not known (cannot be estimated from the available data).

Within each grouping, adverse reactions are presented in order of decreasing seriousness.
Relative epidemiological risk based on local and traveller data Kenya

<table>
<thead>
<tr>
<th>Condition</th>
<th>Frequency</th>
<th>Source</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diarrhoea (est.)</td>
<td>25%</td>
<td></td>
</tr>
<tr>
<td>Influenza</td>
<td>2%</td>
<td>+</td>
</tr>
<tr>
<td>Motorbike injury</td>
<td>84:10,000</td>
<td>*</td>
</tr>
<tr>
<td>Road traffic injury</td>
<td>30:100,000 veh.</td>
<td>*</td>
</tr>
<tr>
<td>Malaria</td>
<td>8:100,000</td>
<td>~</td>
</tr>
<tr>
<td>Stroke</td>
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</tr>
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<td>Enteric fever traveller</td>
<td>0.05:100,000</td>
<td>+</td>
</tr>
<tr>
<td>Enteric fever local</td>
<td>5:100,000</td>
<td>*</td>
</tr>
<tr>
<td>Yellow Fever infection</td>
<td>&lt;1:5 million</td>
<td>?</td>
</tr>
</tbody>
</table>

Key:
* Local pop. data
+ published not country specific
~ calculated on published data
? estimated

a Belderok 2 010 BMC infection., b Coronary Heart Disease Statistics, 2010. BHF. WHO Road Safety 2013
### Vaccine Preventable diseases

<table>
<thead>
<tr>
<th>Disease</th>
<th>Incidence per 2 weeks</th>
</tr>
</thead>
<tbody>
<tr>
<td>LT, LT/ST, mixed-ETEC, “usual” high risk TD</td>
<td>30%</td>
</tr>
<tr>
<td>Influenza A or B</td>
<td>1%</td>
</tr>
<tr>
<td>Typhoid (South Asia)</td>
<td>0.1%</td>
</tr>
<tr>
<td>Hepatitis A</td>
<td>0.01%</td>
</tr>
<tr>
<td>Tick borne encephalitis (exposed in rural</td>
<td>0.001%</td>
</tr>
<tr>
<td>Austria)</td>
<td></td>
</tr>
<tr>
<td>Hepatitis B</td>
<td></td>
</tr>
<tr>
<td>Typhoid (most other destinations)</td>
<td></td>
</tr>
<tr>
<td>Cholera</td>
<td>0.001%</td>
</tr>
<tr>
<td>Japanese encephalitis</td>
<td>0.0001%</td>
</tr>
<tr>
<td>Meningococcal disease</td>
<td></td>
</tr>
<tr>
<td>Rabies</td>
<td></td>
</tr>
<tr>
<td>Poliomyelitis</td>
<td></td>
</tr>
</tbody>
</table>

Steffen, Behrens et.al. Vaccine preventable travel health risks: What is the evidence and how good is it? JTM 2014
UK imported S Typhi and estimated Hepatitis A
Hepatitis A
Travellers Risk

USA+

♦ Travellers 20 million = 1 per 104,000

UK †

♦ Travellers 6.5 million = 1:118,000

♦ Research estimates *&
  ♦ 0.7-28.0 per 100,000 pa (~70-100 cases year)
  ♦ 1 per 3,000 - 17,000 travellers &

* Askling et.al. JTM 2009 & Mutsch et.al CID 2006
+ CDC notifications † PHE Hepatitis A Laboratory notifications ‡ Lu et al. Vaccine 2013
Typhoid rates in travellers.

UK.
- ISC: 17 per 100,000 visits
  - VFR v Non-VFR (RR) of 3.52
- Rest of the world: 0.05 per 100,000 visits

USA. (1999-2006)
- ISC: 9 per 100,000 visits
- Rest of world: 0.02 per 100,000 visits
- Africa: 0.08 per 100,000 visits

Enhanced surveillance of enteric fever.. 2006-2007 HPA
Lynch et al. JAMA 2009
Indirect cost of administering vaccine (not shown)

= vaccine costs Behrens & Roberts BMJ 1994

Prescription Cost Analysis (PCA) Data NHS Wholesale vaccine purchase cost
Yellow Fever Vaccine

Used since early 1950’s
17D line (17D–204 and 17DD)
Grown on fertilised eggs
Deaths from Yellow fever vaccine and natural infection in travellers

Table 1. Cases and deaths, naturally acquired yellow fever and yellow fever vaccine-associated viscerotropic disease, in travelers from the USA, Europe, Australia, Japan and China.

<table>
<thead>
<tr>
<th>Disease</th>
<th>Interval (years)</th>
<th>Cases (n)</th>
<th>Deaths (n)</th>
<th>Case fatality (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>YEL-AVD</td>
<td>1973–1989</td>
<td>2</td>
<td>1</td>
<td>50</td>
</tr>
<tr>
<td></td>
<td>1990–2010</td>
<td>31</td>
<td>12</td>
<td>39</td>
</tr>
<tr>
<td>YF (natural infection)</td>
<td>1990–2010</td>
<td>6</td>
<td>6</td>
<td>100</td>
</tr>
</tbody>
</table>

YEL-AVD: Yellow fever 17D vaccine-associated viscerotropic disease; YF: Yellow fever.

Monath T: Review of the risks and benefits of yellow fever vaccination including some new analyses
A 44 year old professional is planning to travel for a 2 week holiday with family to Kenya. Born in East Africa but now British resident

Will spend 7 days on the Beach and 5 days on Safari and a few days in Nairobi

Immunised YF, typhoid /Hepatitis A, DTP and Cq+PG prophylaxis

Departed Kenya 9 days later
3 days into holiday he experienced back pain and pins and needles in lower limbs. The symptoms became progressively worse requiring a premature return to Nairobi. An MRI scan showed myelitis or demyelination. Required ITU, then an air-ambulance to UK. 2 months later returned home with significant disabilities.
Yellow fever vaccine

- Litigation: lack of informed consent on the risk of YEL-AND with vaccine

While yellow fever vaccination should be encouraged as a key prevention strategy, it is important to screen travel itineraries and carefully evaluate the potential risk of systemic illness after yellow fever vaccination. Great care should be exercised not to prescribe yellow fever vaccination to individuals who are not at risk of exposure to infection, based on an accurate assessment of the travel itinerary. Although vaccination is generally not recommended for travellers going to areas where the risk of exposure is low, any risk (e.g. as a result of prolonged travel or heavy exposure to mosquito bites) should be weighed against individual risk factors for vaccine-associated adverse events (e.g. altered immune status).
<table>
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<tr>
<th>Visits</th>
<th>Serious / Fatal vaccine AE annually est.</th>
</tr>
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<tr>
<td>UK residents ~ 174,000</td>
<td>1-2</td>
</tr>
<tr>
<td>&gt; 55 years old ~ 25%</td>
<td></td>
</tr>
<tr>
<td>All Overseas Visitors</td>
<td>2-4</td>
</tr>
<tr>
<td>1.7 million (KTO) ~ 70% vaccine naïve</td>
<td></td>
</tr>
<tr>
<td>2.8 million visits to Game Parks</td>
<td></td>
</tr>
<tr>
<td>Travel associated Yellow Fever cases</td>
<td>Nil</td>
</tr>
<tr>
<td>1950’s – 2010</td>
<td></td>
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http://www.tourism.go.ke/ministry.nsf/pages/facts_figures
Hepatitis B risk in SHORT term travellers
what is the true risk and current practice?

Australia: HBV infection 2.19 per 10,000 traveler-days. 1 case in 361 Australian travellers.
Johnson et.al. Journal of Travel Medicine 2013

Dutch: Estimated incidence 4.5/100,000 travellers, 66% VFR. 3 in short-term tourists all sexual exposure.
“very low risk of contracting HBV “
Sonder et.al. Journal of Travel Medicine

Danish: HBV infection 9 per 100,000 in < 4 weeks (HAV 10:100,000)
Nielsen et.al. Journal of Infection 2012
Sexual activity, injecting drug use, undertaking relief aid work and/or participating in contact sports.
Travellers are also at risk as a result of medical or dental procedures carried out in countries where unsafe therapeutic injections (e.g. the re-use of contaminated needles and syringes without sterilisation) are a risk factor for hepatitis B (Kane et al., 1999; Simonsen et al., 1999)

3 Reports in the literature of parenterally acquired Hepatitis B since 1987
Severe Anaphylaxis incidence 1.1 per 10^6
?Increased risk of Multiple Sclerosis
Deciding risks without evidence

- Unknown effectiveness of intervention
  - Consultation
  - Outbreak information & diseases updates
- Unknown incidence (rabies, HIV, TB, and crime & injury)
- Impact of intervention versus illness
- Benefit of intervention v risk of intervention
What are the serious & life threatening problems of travellers?
### Relative epidemiological risk based on local and traveller data Kenya

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- BHF. WHO Road Safety 2013.
Use a proxy such as deaths for severe illness during travel
Causes of deaths in Travellers when abroad

Hargarten, 1988; Paixao, 1991; Hargarten, 1985; Frame, 1992, Lunetta 2010
No evidence for differential risk associated with

- Rural or Urban travel
- Accommodation: Hotel, tent or village rooms
- Type of traveller other than VFR and long term travel? Expatriate? Business
Shared decision-making

- Particularly when:
  - Scientific evidence is lacking on risk, or benefits are ‘marginal’
  - A fully informed patient might choose either to have the intervention, or not
  - Patients’ values and preferences contribute to decisions

- But:
  - Accept irrational choice (e.g. VFR not take phxs)
  - Financial considerations affect decisions
The Risk Assessment

- The assessment needs to reflect the health risks and not the interventions available
- Prioritise risks and select order of discussion
  - Common, treatable/avoidable, potentially fatal
- The assessment needs to be tailored to the individuals personal risk values or threshold
- Risk based on **best evidence** not perception or intuition
Risk Thresholds are important
Risk thresholds are important
Does a travel clinic consultation reduce illness in travellers?
### Malaria knowledge of departing passengers by source of advice

<table>
<thead>
<tr>
<th>Source of Advice</th>
<th>Prophylaxis</th>
<th>Score by None</th>
<th>mean Malaria Knowledge Score, max 100</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>no</td>
<td>None</td>
<td>71.7</td>
</tr>
<tr>
<td></td>
<td>yes</td>
<td>non-professional</td>
<td>70.0</td>
</tr>
<tr>
<td></td>
<td></td>
<td>professional</td>
<td>70.0</td>
</tr>
</tbody>
</table>

Behrens & Alexander  Mal. J. 2013
Evidence

Size and Quality of research matters more than research results

1. Evidence based (RCT or CT)
2. Surveillance epidemiology
3. Observational studies
4. Based on case series
5. Based on expert(s) assessment
A frequent flyer as a tourism co-coordinator

Itinerary: Travel on business to Morocco, Kenya, India and Sri Lanka for 3 weeks.

History: Up to date vaccines; needs malaria Phxs.
- H/O 6/12 previously- depression and labile emotional symptoms. Rx with Sertraline and counselling
- Seen by practice nurse and Px mefloquine for Kenya and chloroquine & proguanil for India. (signed by practice partner)

No record of advice or discussion with the traveller
A frequent flyer as a tourism co-coordinator

- The traveller took the first dose of mefloquine around the 2 weeks before departure but aborted travel after Morocco.
- 3 months later presented with symptoms of depression requiring Rx with Sertraline.
- Litigation against practice partner for mefloquine induced depression and negligence on advice and discussion of side effects of mefloquine.

Patients with a history of psychiatric disturbances (including depression) or convulsions should not be prescribed Lariam prophylactically, as it may precipitate these conditions (see 4.4 Special warnings).
Risk management

- Nurse knowledge & education & PGD
- Practice audit QC and competence on prescribing
- Note keeping of consultations
A VFR family

- A Nigerian mother with a 3 month infant seeks travel advice for their visit to family in rural Nigeria. They plan to be away for 4 weeks. The mother is breast feeding and has last visited Nigeria 2 years previously.

- What further advice should be given?
A VFR family

• The advice from a practice nurse is that the child is too young for malaria prophylaxis and the mother, as she is breast feeding the child, cannot take chemoprophylaxis.

Who agrees with this advice
Guidelines for malaria prevention in travellers from the UK 2014

- The small amounts of antimalarials that pass into breast milk are not enough to protect the baby. Breastfeeding infants therefore need to take their own prophylaxis.

- If travel is unavoidable, infants and children should be well protected against mosquito bites and receive appropriate malaria chemoprophylaxis.

Early diagnosis

- 41 year old Caucasian male
- Recent travel to Gambia – returned 2 weeks before
- Seen by GP
  - 5 days after return with symptoms of diarrhoea; given supportive advice,
  - 12 days later;
    - diagnosed with bronchitis and Rx amoxicillin
- Presented to DGH 14 days after return
  - H/O recent travel and no prophylaxis
Presentation to hospital 2 weeks after return

- `Flu-like symptoms`
- Jaundice
- Drowsy
- Temp 35.6 BP 104/82
- Pulse 110 RR 28
- Icteric
- `Encephalopathic`
- GC Score 7
Lab and Rx 2 weeks after return

- Hb 11.00 gm/l plt 19.0 $10^9$
- Na 119 K 4.1
- Malaria parasites 15% Pf.

Rx
- Artesunate I.V. & 6 unit exchange transfusion
Progress and Outcome

- BP continued to fall
- Acute tachycardia with hypotension
- Persistent hyperkalemia despite haemofiltration & insulin
- Persisting hypotension & hyperkalemia
- QRS widening on ECG
- 4 organ failure
- Arrested and died 17 days after return
Delay to diagnosis in fatal P. falciparum malaria in French patients 1996–2003 (n = 21,888)

<table>
<thead>
<tr>
<th>Time from onset to diagnosis</th>
<th>Fatality rate/1000</th>
<th>Odds Ratio</th>
</tr>
</thead>
<tbody>
<tr>
<td>0–1 d</td>
<td>2</td>
<td>1</td>
</tr>
<tr>
<td>2–3 d</td>
<td>3</td>
<td>2</td>
</tr>
<tr>
<td>4–6 d</td>
<td>6</td>
<td>3</td>
</tr>
<tr>
<td>&gt;6–14 d</td>
<td>6</td>
<td>4</td>
</tr>
</tbody>
</table>

p = 0.005

Legros et al. EIDi 2007
Running a Travel Clinic in primary care

- More than a PGD
  - Competence (training) in risk assessment
  - Informed consent (does not need a signature)
  - Lead GP needs TH knowledge for monitoring quality and auditing practice
  - Keep record of consult - must be able to replicate discussion from the notes
  - Drugs and vaccines can cause significant harm to healthy individuals
NHS referral service at the HTD Travel clinic

NHS commissioned service for travellers with pre-existing or complex health problems

- Cancer, cardiovascular, diabetic, rheumatologic & respiratory problems.
- Immunocompromised, allergies, adverse reactions to drug, vaccines.
- High risk travellers: infants & children, elderly travellers (=>65yrs.), expatriates (> six months) and pregnant women

Hours: Wednesday 1pm-4pm, Thursday 9am-4pm and Fridays 9am-1pm. Telephone Bookings: 020 3447 5999