The RAGIDA project
European Risk Assessment Guidance for Diseases transmitted on Aircrafts

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What is ECDC?

An independent agency, named the European Centre for Disease Prevention and Control ... ECDC Founding Regulation (851/2004)

A European Union Agency which:

- covers EU 27, EEA/EFTA countries;
- reaches out to other countries beyond the EU 27 through Neighbourhood Policy and DG RELEX;
- supports and promotes global health security (role in International Health Regulations);
- is financed through the EU budget.

- according to the Article 3 of the Founding Regulation, ECDC's mission is to identify, assess and communicate current and emerging threats to human health posed by infectious diseases.
Travel to Europe in May 2007

Atlanta-Paris-Athens-Mykonos-Athens-Rome-Prague-Montreal

Diagnosed as extensively resistant tuberculosis (XDR-TB)

The Speaker case-study - 2007

US-CDC engages in extensive contact tracing

The patient... is relatively asymptomatic...
The Speaker case-study – 2007
Overview contact tracing

US: no evidence of transmission or active disease among 6 family contacts, 20 friends/family/co-workers, 10 health care workers

Europe: no evidence of transmission or for active disease among screened passengers

<table>
<thead>
<tr>
<th>COUNTRY</th>
<th>Passengers in rows “2-1-2”</th>
<th>“Concerned Crew”</th>
<th>Persons to be traced</th>
<th>Persons contacted</th>
<th>Persons tested</th>
<th>Initial +ve TST results</th>
<th>Initial -ve TST results</th>
<th>X-ray result</th>
</tr>
</thead>
<tbody>
<tr>
<td>France</td>
<td>7</td>
<td>5</td>
<td>12</td>
<td>11</td>
<td>6</td>
<td>3</td>
<td>3</td>
<td>2 normal, 1 old TB</td>
</tr>
<tr>
<td>Greece</td>
<td>1</td>
<td>0</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>0</td>
<td>normal</td>
</tr>
<tr>
<td>Hungary</td>
<td>1</td>
<td>0</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>0</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>United Kingdom</td>
<td>1</td>
<td>0</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>0</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>Czech Republic</td>
<td>6</td>
<td>13</td>
<td>19</td>
<td>17</td>
<td>17</td>
<td>13</td>
<td>4</td>
<td>normal</td>
</tr>
<tr>
<td>Romania</td>
<td>3</td>
<td>?</td>
<td>3</td>
<td>3</td>
<td>?</td>
<td>?</td>
<td>?</td>
<td>?</td>
</tr>
<tr>
<td>Total</td>
<td>19</td>
<td>18</td>
<td>37</td>
<td>34</td>
<td>26</td>
<td>17</td>
<td>9</td>
<td></td>
</tr>
</tbody>
</table>

The Speaker case-study – 2007
Lesson’s learnt

→ Revision of the WHO guidelines for Tuberculosis and air travel

→ Start of the RAGI DA project .....  

Objectives:

- to assist Member States in the evaluation of risk for the transmission of various infectious agents on board of aircrafts
- to assist the national public health authorities in determining which passengers, crew and other staff possibly at risk should be contacted and informed on their possible exposure to an infectious passenger
RAGI DA part I
Literature review and expert consultation

Robert Koch Institute, Germany was commissioned to perform a systematic review of peer-reviewed and grey literature for the following 12 diseases:

- Tuberculosis
- SARS
- Meningococcal diseases
- Influenza
- Measles
- Rubella
- Diphtheria
- Ebola and Marburg hemorrhagic fever
- Lassa fever
- Smallpox
- Anthrax

RAGI DA part I - Methods

Standardized interviews
- with PH experts of the EU Public Health agencies and Aviation boards

Systematic review of guidelines addressing risk assessment and management to air passenger travel
- Aviation boards, the Airport Council International (ACI), International Air Transport Association (IATA) and International Civil Aviation Organisation (ICAO)
- Web-based publications of national and international public health agencies (WHO, CDC, HPA, Heath Canada, RKI)

Compilation of pathogen specific epidemiologic attributes
- such as R0, incubation period, period of shedding, period of maximum an minimum infectiousness, signs and symptoms increasing transmissibility and pre-vaccination immunity
**Evidence of transmission**

<table>
<thead>
<tr>
<th>Disease</th>
<th>Events</th>
<th>Peer reviewed</th>
<th>Grey literature</th>
<th>Interviews</th>
<th>Time frame</th>
<th>On board transmission</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tuberculosis</td>
<td>28</td>
<td>18</td>
<td>4</td>
<td>6</td>
<td>1992-2008</td>
<td>6</td>
</tr>
<tr>
<td>Influenza</td>
<td>5</td>
<td>5</td>
<td>-</td>
<td>-</td>
<td>1977-1999</td>
<td>4</td>
</tr>
<tr>
<td>SARS</td>
<td>9</td>
<td>9</td>
<td>-</td>
<td>-</td>
<td>2003</td>
<td>4</td>
</tr>
<tr>
<td>Meningococcal disease</td>
<td>9</td>
<td>4</td>
<td>2</td>
<td>3</td>
<td>2000-2008</td>
<td>1</td>
</tr>
<tr>
<td>Measles</td>
<td>6</td>
<td>6</td>
<td>-</td>
<td>-</td>
<td>1981-2005</td>
<td>5</td>
</tr>
<tr>
<td>Ebola VHF</td>
<td>1</td>
<td>-</td>
<td>1</td>
<td>-</td>
<td>1996</td>
<td>0</td>
</tr>
<tr>
<td>Lassa VHF</td>
<td>7</td>
<td>3</td>
<td>1</td>
<td>3</td>
<td>2000-2006</td>
<td>0</td>
</tr>
<tr>
<td>Smallpox</td>
<td>3</td>
<td>1</td>
<td>-</td>
<td>2</td>
<td>1970</td>
<td>0</td>
</tr>
</tbody>
</table>

**RAGI DA part I - Results**

- Very limited information is available for the majority of diseases
- Only single events are published in peer-reviewed journals
- Evidence base for disease transmission onboard aircrafts is weak
- Limited national guidance, not consistent between EU Member States
- Except for tuberculosis, no international guideline for contact tracing exists

RAGI DA part II – Operational disease specific guidance for contact tracing

2009 a first expert consultation on
• Tuberculosis
• SARS
• Invasive Meningococcal infections

2010 a second expert consultation on
• Measles
• Rubella
• Viral hemorrhagic fever
• Anthrax and Smallpox

• Small, multidisciplinary expert panels
• Review of evidence and expert assessment
• Expert’s validation and consensus building


Example - Tuberculosis

1. Literature review

• Events identified: 28 (1992 - 2008)
  o 18 events published in 11 peer reviewed articles
  o 4 event articles published in grey literature
  o 6 events identified through expert interviews

• Evidence base limited
  o 3 events with evidence of tuberculin skin conversion
    ▪ 1 crew to crew
    ▪ 1 from high incidence country (boosting not excluded)
  o No tuberculosis has been described as a consequence of transmission on board

• Contact tracing (CT) rather ineffective
  o 3677 contacts identified (72% passengers, 10% crew); low estimate
  o CT could successfully trace 48.4% of the identified contacts
Example - Tuberculosis

2. Suggested approach and criteria to be considered:

The index case

- **Index case with confirmed infectious pulmonary TB:** Defined as culture or molecular probe-confirmed cases with positive sputum smear microscopy (including induced sputum or bronchoalveolar lavage);
- **The infectiousness of the index case:** Evidence of transmission in other settings, such as transmission to household members or other close contacts.

Effective exposure

- **Duration of flight:** Flight duration equal to or exceeding eight hours of flight time including ground delays (www.flightstats.com);
- **Location onboard:** Evidence for onboard TB transmission is very low for passengers seated more than two rows ahead or two rows behind the index case; therefore, contact tracing is only recommended for passengers sitting in the same row, two rows ahead and two rows behind the index case.

Example - Tuberculosis

3. Algorithm

```
Incident reported
Patient with infectious pulmonary TB? 
Yes  No  No contact tracing
Evidence of transmission to close contacts (household and other close contacts)?
Yes  No  No contact tracing
Flight duration 8 hours or longer? 
Yes  No  No contact tracing
Flight took place less than 3 months ago? 
Yes  No  No contact tracing
Trace contacts in the same row and two rows ahead and two rows behind the index case
```

*Infectious pulmonary TB: defined as culture or molecular probe-confirmed cases with a positive microscopy sample (i.e., including induced sputum or bronchoalveolar lavage)*
**Example - Tuberculosis**

4. Question & answer template

1. When should contact tracing be considered?
2. When is a patient infectious?
3. Who should be considered for contact tracing?
4. Are there special considerations for MDR/XDR TB?
5. Are there special considerations for individuals of higher susceptibility?

**RAGIDA part III - update and revision**

1. Web-based survey

   Survey send to 318 email addresses/persons
   – Members of the ECDC Advisory Forum
   – ECDC Competent Bodies
   – Contributors/participants of the RAGIDA part I, part II
   – CAPSCA members
   – Members of the AIRSAN project
   – Ministries of Transportation
   – Civil aviation authorities
   – International bodies (WHO, IATA, ICAO.....)

   Response rate = 36%
Some suggestions ...

- Add chapters on Influenza (novel), SARS, novel CoV, Avian influenza
- Add chapter on respiratory infections /syndromic approach SARI
- Involve aviation medical experts in revising the guidelines;
- Address logistical problems (time to get passenger contact information/data protection) in the decision making process for effectiveness of control measures
- Join WHO's and ICAO's joint CAPSCA forum to develop further your outcome

RAGIDA part III - next steps

2. Literature review


- Disease specific working groups on tuberculosis, measles, influenza, coronavirus infections as well as a joint group on acute respiratory infections

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Viral hemorrhagic fevers expert group: Roberta Andraghetti, Ray Arthur, Andreas Gilsdorf, Stephan Günther, Michel van Herp, Katrin Leitmeyer, Diiys Morgan (chair), Aura Timen, Maggie Tomlinson.

Discussion (1)

Evidence

Existing evidence base has several limitations

- Small number of studies reported on a limited number of events
- Observational studies lacking appropriate controls and no control for biases
- Definitions of “contact” vary
- Proportion of passengers (contacts) successfully traced is small
- Asymptomatic carriers are likely to be undetected
- Studies without evidence for transmission are less likely to be published
Discussion (2)

Evidence -> Risk assessment

- Based on probability and impact but also on risk perception
- Epidemiological situation in country of origin and destination
- Susceptibility of population
- Maximum incubation period / period for intervention
- Measures for intervention

Recommendation

Discussion (3)

Evidence -> Risk assessment

- Contact tracing is resource intense and the feasibility is limited by national or aviation regulation
- Cost benefit of contact tracing unknown/needs to be better studied
- Ethical aspects (containment/mitigation measures acceptable)

Recommendation