Hepatitis A outbreak among European travelers returning from Egypt

by

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on behalf of

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Epidemiology of Hepatitis A in Germany

- Notifiable disease
  - Incidence 1.5 / 100,000 (2005/2006)
  - Highest incidence in children 5-9 years
  - Notifications peak after summer holidays

- 40% travel associated
  - 60% acquired in Germany

- Vaccination:
  - Not universally recommended, but for
    - Risk groups (e.g., contacts, occupational or individual risk)
    - Travelers to endemic areas
  - Travelers often not adequately informed and vaccinated
Identification of the outbreak

- Local health dept. noticed 4 cases, all guests of the same hotel in Hurghada, Egypt (Aug 13th, 2004)
- Hotel did not know – disease onsets after departure
- RKI => information of all local health depts.

- Case numbers rose exponentially within days
Extent of the outbreak: 351 cases in 9 countries

- **Germany:**
  - 271 primary cases, guests of hotel X
    - age: 2-67 years, median 34 years
    - 54% male
  - 7 secondary cases, persons who had not traveled but were infected in Germany by guests of hotel X

- **Elsewhere in Europe** (A, S, DK, NL, B, I, CH, GB):
  - 60 primary cases
  - Secondary outbreak with 13 cases in Austria
Outbreak setting

- Egypt highly endemic for hepatitis A
- Hurghada – Red Sea resort
  - Hotel employees from Nile valley
  - Supplies (foods etc.) basically all transported in
- Hotel X:
  - ‘all-inclusive’ hotel, 550 rooms
  - pools, beach access
  - 2 breakfast rooms, 3 restaurants, 5 bars
  - good reviews, many returning guests
Timing of the outbreak

- Infected guests in hotel: June 9th to August 6th
- Min. period with infections: June 24th to July 23rd
- Symptom onset: July 10th to September 8th

![Graph showing symptom onset and secondary cases among travelers]
Measures and investigation

- Information about the outbreak:
  - Hotel and Egyptian government
  - Other countries possibly affected
  - Hotel guests, the public

- Egypt:
  - Serological examination of the hotel’s employees
  - Hepatitis A vaccination offered to current hotel guests
  - Hotel kitchen inspected (as to hygiene)
  - Change of some food suppliers
  - Investigation of suppliers

- Germany:
  - Travel agents offered alternative package holidays
  - Virological investigation (sequencing)
  - Case-control study regarding source(s) of infection
Hypotheses regarding source(s) of infection

3 Hypotheses:

Disease associated with the consumption of...

• ... ice cream (served daily)
• ... orange juice (breakfast)
• ... salads, raw vegetables (buffet)

Also studied:

• Consumption of tap water (ice cubes, using tap water for dental hygiene)
• bathing habits (pool, ocean), day trips
• Other foods, drinks
Case-control-study: Methods

- **Participants:**
  - Guests of hotel “X”, at least one day 6/24 through 7/23
  - >17 years of age, one person per household

- **Cases:** registered cases

- **Controls:** Healthy travelers who
  - were not vaccinated against hepatitis A and
  - did not recall previous hepatitis A infection

- Standardized telephone interviews, conducted by local and state health departments, RKI
Case-control-study: Results

No difference between groups regarding:
- age, sex
- consumption of ice cream, salads
- excursions, bathing habits, etc

But:

<table>
<thead>
<tr>
<th></th>
<th>Cases n=69</th>
<th>Controls n=36</th>
<th>OR</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Orange juice / breakfast</td>
<td>82.3%</td>
<td>63.9%</td>
<td>2.6</td>
<td>1.1-6.6</td>
</tr>
<tr>
<td>Days drinking orange juice</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>0 days (Reference)</td>
<td>17.7</td>
<td>36.1</td>
<td>Ref.</td>
<td>-</td>
</tr>
<tr>
<td>1-6 days</td>
<td>13.2</td>
<td>30.5</td>
<td>0.9</td>
<td>0.3-2.9</td>
</tr>
<tr>
<td>7-13 days</td>
<td>32.4</td>
<td>16.7</td>
<td>4</td>
<td>1.2-13.1</td>
</tr>
<tr>
<td>14+ days</td>
<td>36.8</td>
<td>16.7</td>
<td>4.5</td>
<td>1.4-14.8</td>
</tr>
</tbody>
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On-site investigations

- **Hotel:**
  - No employee with IgM-antibodies against hepatitis A
  - Little fluctuation of staff
  - Kitchen: no hygiene problems

- **Investigations of suppliers focused on juice producer**
  - Hygiene problems at site of production
  - No employee IgM-positive at time of investigation, but substantial fluctuation
  - No license to supply international hotels
  - No other customers (hotels) in Hurghada
  - Juice not heat-treated (pasteurized etc.)
Virological investigation

42 serum samples
Nested PCR (VP1/2A, 340 bp)

n=22 PCR+ for HAV RNA

HAV sequences (n=13): all identical genotype 1B

(routine) monitoring of circulating HAV strains useful to:
- detect widely dispersed outbreaks and hidden clusters
- demonstrate links between imported and autochthonous cases
Discussion, conclusions

- Largest ever described hepatitis A outbreak among tourists / travelers
- Orange juice most likely vehicle of infection
  - Case-control-study
  - On-site investigation
- Outbreak investigation difficult
  - long incubation period (15-50 days)
  - large number of cases
  - almost impossible to test food or water for hepatitis A virus
- Many tourists to Egypt not vaccinated
  - travel operators should inform (catalogues)
  - tourists need to seek competent advice pre-travel
Update....

1. Since last year: increasing number of health plans cover Hepatitis A vaccination for travelers.

2. Lately, while booking online...

Tour operators notice:
...flight plan...
...double room, bathroom, balcony...

We would like to point out that travelers to Egypt are advised to be vaccinated against hepatitis A and to seek information on the general vaccination recommendations.
Many thanks to...

...all participants of the case-control-study,
...local and state health departments,
...collaborators in other affected countries,
...the Egyptian authorities,
...many colleagues in the Department for Infectious Disease Epidemiology of the RKI.

Reference: Frank et al.  
Major outbreak of hepatitis A associated with orange juice among tourists, Egypt, 2004.  