Challenges and opportunities in risk assessment for viruses

Marion Koopmans  @MArionKoopmans
Estimates of foodborne viral disease, US

**Estimated nr FB cases Per 100000**

- NoV: 2707
- Bacteria: 1808
- Viruses: 1785
- Parasites: 1181

**Estimated nr hospitalisations**

- NoV: 53414
- Bacteria: 35796
- Viruses: 21519
- Parasites: 23962

**Estimated nr deaths**

- NoV: 1761
- Bacteria: 861
- Viruses: 260
- Parasites: 245

99% NoV

95% NoV

95% HAV

Scallan et al., 2011
<table>
<thead>
<tr>
<th>Category</th>
<th>Source</th>
<th>Mode of Tx</th>
<th>Example</th>
<th>Clinical syndrome</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fecal viruses human</td>
<td>Fecal contamination at source irrigation Food handler</td>
<td>Fecal oral</td>
<td>Norovirus Sapovirus Astrovirus Rotavirus Enterovirus <strong>Hepatitis A virus</strong> Hepatitis E virus? .....</td>
<td>Diarrheal disease Hepatitis Neurological disease</td>
</tr>
<tr>
<td>Fecal viruses animal</td>
<td>Fecal contamination at source Irrigation (shellfish, berries)</td>
<td>Fecal oral, zoonotic</td>
<td>Hepatitis E virus Rotavirus .....</td>
<td>Hepatitis Diarrheal disease</td>
</tr>
<tr>
<td>Systemic infection animal</td>
<td>Meat, animal products</td>
<td>Zoonotic, including fecal oral</td>
<td>Hepatitis E virus TBE Nipah Avian influenza Rift valley fever MERS ....</td>
<td>Hepatitis Neurological disease Respiratory disease Hemorrhagic fever ....</td>
</tr>
</tbody>
</table>
Issues to address in microbial risk assessment

- Microbial growth and death
- Genetic diversity and evolution
- Potential for secondary transmission
- Immunity
- Diversity of health endpoints
- Heterogenous distribution in environment
- Detection method sensitivity
- Population, community, and ecosystem level dynamics
- Routes of exposure
- ...
- Infectome, microbiome and exposome

Family, genus, genogroups, genotypes, variants

Clade GII
~80%
Seasonal HCAI

Dominant Variant (GII.4)

Clade GGI
~20%
More varied Food

Clarke et al, 2010; Verhoef et al., 2011; Kroneman et al., 20
Evidence for QMRA

- Prolonged shedding, more time for genetic evolution, less immune pressure

Transmission via food (non-GII.4) via person-to-person contact (GII.4)

- Genetic and antigenic evolution due to immune pressure

De Graaf et al., submitted
Noroviruses persist in the population through evolution

Effects of mutations:

Escape mutants (drift)
- No protective immunity

Differences in host cell binding
- New host range

Siebenga et al., 2008; Allen et al., 2008; Parra et al., 2012; Tan et al., 2003
Lindesmith et al., 2008; Bok et al., 2009; Siebenga et al. 2010
Reassortment

- Infection of a single cell with more than one strain > progeny virus with mixed genome
- More likely when humans are exposed to multiple viruses
  - Eg foodborne outbreaks
  - Daycare centres
  - Immunocompromised persons
- Potential for introduction of novel viruses into the population (mixed genomes)

De Graaf et al., submitted
Emergence of recombinant strains may change impact

Kenya 2012-2013, environmental

China, Japan 2014-2015, outbreaks

De Graaf et al., 2015; van Beek et al., submitted
Great fluctuations in estimated foodborne illness

Verhoef et al., 2015
Sequence based cluster detection, HAV example

France: Jan 2010
N = 59 cases HAV infections

The Netherlands: Jan 2010-2011
N = 14 cases HAV infections

Nordic countries: Oct 2012 - 2013
N = 103 cases HAV infections

Semi-Dried tomatoes

Frozen Berries

Australia: May 2009
N = 250 cases HAV infections

Petrignani et al., 2010, 2014
Hurdle: getting robust evidence for foodborne outbreaks

Figure 24: Time line of deliveries from “hotspot” PL#98 to lots and cases in Italy, Ireland and Sweden (only confirmed cases are represented)
Intensive farming under scrutiny as French oysters face viral wipeout

From Hugh Schofield in La-Trinité-sur-Mer, Brittany
6 Jun 2010

French oyster farmers are facing ruin after a viral epidemic – which many believe is linked to intensive farming methods – struck for the third year in a row, wiping out millions of the baby shellfish.

From the Mediterranean coast, up to the Bay of Arcachon on the Atlantic and now Brittany, farmers have watched in dismay in recent weeks as the virus once again moved northwards, keeping pace with the rising sea temperature.

In 2008 and 2009 the industry was ravaged by the same epidemic, with many farms losing 80% to 100% of their stocks of oysters – first-year baby oysters. Because it takes three years to grow a commercially viable oyster, so far the economic impact of the crisis has been limited.

But now all pre-2008 production has been depleted, so major shortages are predicted next winter when demand peaks around Christmas and New Year. In France that is when 80% of oysters are sold.

The Committee to Save Oyster-Farming – an ad-hoc group set up in answer to the crisis – has warned that 40% of the country’s 4,800 mainly family-run businesses could be forced to close, with the loss of thousands of jobs.

"Unofficially everyone thinks the hatcheries are to blame, even if no-one says so openly."

Jacques Cabaret

Oysters have been hit by the Osh-N1 virus

Market shift

Top producers: China, Japan, Korea
Emerging viruses and the food chain

- Pig Hepatitis E – *immunocompromised*
- SARS – wild animal markets
- Nipah – fruits > pigs > people
- Avian influenza – food handlers, blood
- Rift valley fever – animal products, slaughter
- Ebola – bush meat
- MERS coronavirus: dromedary milk, slaughterers – *immunocompromised*
- .......
Impact of avian influenza H7N9 emergence

KFC China Same Store Sales (2013)

% Change

Source: Yum Brands
A global platform for the sequence-based rapid identification of pathogens - Start date December 1\textsuperscript{st} 2014

Coordinated by
Frank M. Aarestrup (Technical University of Denmark)
Marion Koopmans (Erasmus Medical Center, the Netherlands)

www.compare-europe.eu
Analytical framework and globally linked data and information sharing platform.

RA Models & risk-based strategies
for sample and data collection

Harmonized standards
for sample processing and sequencing

Analytical workflows
for generating actionable information

Data and information platform
The future of risk assessment science for viruses?

Develop capacity to deal with emerging diseases > agenda setting for research
Develop capacity to take stock of evolving data sources