Food-borne viruses

Marion Koopmans

Professor of public health virology
<table>
<thead>
<tr>
<th>Virus group</th>
<th>Families</th>
<th>Foodborne</th>
</tr>
</thead>
<tbody>
<tr>
<td>dsDNA</td>
<td>African swine fever-like viruses, Hepadnaviridae, Papovaviridae, Iridoviridae, Herpesviridae</td>
<td>Poxviridae, Adenoviridae</td>
</tr>
<tr>
<td>ssDNA</td>
<td>Circoviridae</td>
<td>Parvoviridae</td>
</tr>
<tr>
<td>dsRNA</td>
<td>- strand RNA: Rhabdoviridae, Bunyaviridae, Arenaviridae</td>
<td>Orthomyxoviridae, Paramyxoviridae, Filoviridae</td>
</tr>
<tr>
<td></td>
<td>+ strand RNA: Arteriviridae, Togaviridae</td>
<td>Flaviviridae, Hepeviridae, Coronaviridae, Caliciviridae, Picornaviridae, Astroviridae</td>
</tr>
</tbody>
</table>

Z = zoonoses
Grouping of (potential) food-borne viruses by most likely route of exposure

**Group 1**
- Food handler
- End of chain
- High incidence
- Human pathogens
- Local, endemic
- Fecal oral transmission

Agents: Norovirus, Hepatitis A

Products: Berries, ready to eat foods

**Group 2**
- Production
- Early in chain
- High incidence
- Human and animal pathogens
- Globalisation
- Mixed infections > risk
- Fecal oral transmission

Agents: Norovirus, rotavirus, Hepatitis A, hepatitis E, enterovirus

Products: shellfish, irrigated produce

**Group 3**
- Zoonotic
- Early in chain
- Rare
- Globalisation
- Emerging infections
- Oral transmission and food handling

Agents: Hepatitis E, Avian influenza, SARS, Nipah, Ebola

Products: meat, animal products

*Microbial risk assessment series: Viruses in food, WHO 2008*
Underascertainment of food-borne viruses

Group 1:
- No systematic surveillance
- Lack of knowledge in food sector
- Current regulations based on bacterial pathogens
- Indicator organisms poor predictive value for detecting virus problems

Group 2:
- Inequity in surveillance capacity
- No standardisation in laboratory and epidemiological data collections

Group 3:
- No surveillance at human animal interface
The typical diagnostic work-up of a stool specimen in patients with gastro-enteritis: strong bias for bacterial pathogens

Friesema et al., 2007
Physician considers food source (viral)

Lab considers food source

Patient thinks about possible food source

Patient remembers menu
Leftovers available
Analyses positive

Notification of FSA

Reported to Health Dept/CDC

Culture-confirmed case

Lab tests for organism

Specimen obtained

Person seeks care

Person becomes ill

Population survey

Active surveillance

Laboratory survey

Physician survey

Population
Factors to consider when discussing nosocomial norovirus

Health care institution
Drift, recombination

General community
Drift, recombination

Food water

Environmental surfaces

New introductions?

New introductions?

HCW

Visitor

Animals

Environmental contamination
Estimated nr FB cases Per 100000

Estimated nr hospitalisations

Estimated nr deaths

99% norovirus

95% norovirus

95% hepatitis A

Scallan et al., 2011
Participants of noronet (noronet@rivm.nl)

Europe:
Established in 1999 as Integrated lab and epi project study trends and their relevance
Central databases for reporting outbreaks
Since 2006 global, lab-based

Japan network

Australia/NZ network
Databases

Since 1999 the FBVE network has maintained a joint database in which members have shared their data.
First a joint database was made for foodborne outbreaks caused by different viruses. In 2008, using new software, separate databases were set up for different pathogens, of which the norovirus and hepatitis A database are available on the web.

The Norovirus sequences can be searched and compared to new sequences by the network members at the sequence database (participants only).

A public sequence database displaying a subset of the norovirus data is also available.

A similar dataset has been set up with a smaller group of countries, within the FBVE network for Hepatitis A (participants only).

Besides these password protected databases the FBVE network maintains a public typing tool.

The investigation of outbreaks may be limited due to the high numbers of outbreaks reported to a Public Health institution. In order to increase the success-rate of identifying a food-borne source of infection, a transmission mode distinguishing tool (189Kb) was built based on FBVE data as part of a publication.
~80%
Mostly health care associated outbreaks

Limited virus diversity

~20%
More diverse settings
Higher proportion foodborne
greater virus diversity

Limited seasonality

Kroneman et al., 2008
Steep increase in number of reported outbreaks in recent years

Rapid evolution of dominant strains through drift

Increased mortality

High impact and chronic disease in immunocompromised

Siebenga et al., 2010, van Asten et al. 2011
New recombinants introduced in 9 countries via contaminated shellfish

Continued circulation, additional recombination, 4 different capsids

2nd most common infection in hospitalised children
### NoV phylogenetic lineages in Genogroups I and II

<table>
<thead>
<tr>
<th>ORF 2 Genotypes</th>
<th>ORF 1 Genotypes</th>
<th>ORF 2 Genotypes</th>
<th>ORF 1 Genotypes</th>
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<tbody>
<tr>
<td>I.c1</td>
<td>I.p1</td>
<td>II.c1</td>
<td>II.p1</td>
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<td>II.pk</td>
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</table>

- Established NoV genotypes
- Orphan capsid
- Orphan polymerases > new introductions?
Verhoef et al., 2011

Analysis of FBVE NoV outbreak database, capsid data

Molecular approach:

- Define seq clusters
- Compute probability of clustering for given genotype
- Analyse seq clusters for association with food
- Compute P value for food-borne association

Verhoef et al., 2011
Characteristics of source contaminated outbreaks (FBVE network 2007-2010)

- **Verhoef et al., 2010**

- **Increase**
  - Foodborne (source): 20%
  - Foodhandler: 211%
  - Person-to-person: 117%
Surveillance as information for action

Come on! It can’t go wrong every time...
Prevalence of Antibodies to Hepatitis A Virus, 2006

Endemic
Children
Asymptomatic

Epidemic
Adults; May be severe

CDC slide, accessed at http://virology-online.com/presentations/index.htm
Problem for food investigation:
Major challenge for people to remember what they ate 30 days ago
INFOSAN notification:

- November 2009- Australian authorities notified WHO, under the IHR, of a multi-jurisdictional outbreak of hepatitis A affecting over 250 people linked to semi-dried tomatoes
- Epidemiological evidence implicated semi-dried tomatoes
- Traceback investigation was complex but tomatoes imported frozen (!! Shelf-live!!) tested positive

Action: Alert posted on IHR and INFOSAN closed sites
Cluster in France, Nov 2009 – Feb 2010
Epi link to semidried tomatoes
Source unknown

Institute de Veille Sanitaire
http://www.invs.sante.fr/display/?doc=surveillance/hepatite_a/point_vha_020310.htm
Unusual sequence cluster of HAV cases, no increased reporting

Cases of hepatitis A contracted in the Netherlands between 10 December 2009 - 13 April 2010 (n=66)

Onset of disease per week

Count

Nonrelated case
Secondary case not confirmed
Secondary case confirmed
Cases unknown
Primary case confirmed

Petrignani et al., 2010
Analysis of viral sequences

Exact source not identified

Complex distribution chain

FAO field inspection

Recent update: cases in UK and NL

Identical strain

Both trace back to common supermarket chain

No definitive evidence > no action
GENOTYPE 3 HEV in swine herds (pigs 1 to 5 mo of age)

Samples: Avg = 32%
Herds: Avg = 52%

! Over 300,000,000 pigs raised in Europe each year!

GENOTYPE 3 HEV in acute hepatitis patients

Average 7.1%

Widdowson et al. 2007; Boomkens et al., 2005; Rutjes et al., 2009; Herremans et al, 2007
Geographical clustering of human AND animal strains
Sources of infection remain unclear
International agreement of protocols needed
Oyster herpes virus
Massive die-out
Market shift
Top producers: China, Japan, Korea

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 despair 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 70% 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 4,000 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

Irmer – the state marine research agency – described the situation as ‘one of the worst crises in the history of French oyster farming’.

Last month, hundreds of farmers staged a much-publicised protest in central Paris, dumping tons of oyster shells on one of the Seine River bridges. Their pressure paid off, because the French government has now promised a €150 million rescue package to tide the industry over the next three years.

Low tide on the sand flats at Le Po – a hamlet near Carnac in southern Brittany – exposes the patches or bags of oysters being biologically enriched. In the supposedly pristine waters of the estuarine system at the mouth of the River Goyen. The estuary has a large delta that stretches across the river, creating a large area for the growth of oysters.
<table>
<thead>
<tr>
<th>Country (source)</th>
<th>Samples analyzed</th>
<th>% positive</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Asia</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>11 countries</td>
<td>507</td>
<td>10.5% NoV*</td>
<td>Cheng et al., 2005</td>
</tr>
<tr>
<td>China</td>
<td>128</td>
<td>19% NoV</td>
<td>Kou et al., 2006</td>
</tr>
<tr>
<td><strong>Europe</strong></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Netherlands</td>
<td>42</td>
<td>17% NoV</td>
<td>Boxman et al., 2006</td>
</tr>
<tr>
<td>Italy</td>
<td>235</td>
<td>6% HAV, 14% NoV, 2% both</td>
<td>Groci et al., 2007</td>
</tr>
<tr>
<td>Italy</td>
<td>170</td>
<td>14% HAV</td>
<td>Macaluso et al., 2006</td>
</tr>
<tr>
<td>Netherlands</td>
<td>64</td>
<td>22% EV</td>
<td>Lodder et al., 2005</td>
</tr>
<tr>
<td>France</td>
<td>52</td>
<td>40% EV</td>
<td>Dubois et al., 2004</td>
</tr>
<tr>
<td>Spain</td>
<td>60</td>
<td>47% AdV, 19% EV, 24% HAV</td>
<td>Muniaín-Mujika et al., 2003</td>
</tr>
<tr>
<td>France, Netherlands, Ireland</td>
<td>87</td>
<td>9% NoV, 5% EV</td>
<td>Beuret et al., 2003</td>
</tr>
<tr>
<td>Spain</td>
<td>?</td>
<td>27% HAV, 44% EV</td>
<td>Romalde et al., 2002</td>
</tr>
<tr>
<td>Italy</td>
<td>100 before depuration 90 after depuration 100 market</td>
<td>20% (34%***), 11% HAV, 23% HAV</td>
<td>Chironna et al., 2002</td>
</tr>
<tr>
<td>Italy</td>
<td>142</td>
<td>35% (13%)</td>
<td>De Medici et al., 2001</td>
</tr>
<tr>
<td>France</td>
<td>108</td>
<td>17% AV, 23% NoV, 19% EV, 27% RV</td>
<td>LeGyader et al., 2000</td>
</tr>
<tr>
<td><strong>South America</strong></td>
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<tr>
<td>Brazil</td>
<td>27</td>
<td>22% HAV</td>
<td>Coelho et al., 2003</td>
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<tr>
<td>South America</td>
<td>17</td>
<td>24% HAV</td>
<td>Romalde et al., 2001</td>
</tr>
</tbody>
</table>

* NoV = norovirus, HAV = hepatitis A virus, EV = enterovirus, AdV = adenovirus, AV = astrovirus, RV = rotavirus
Genetic profiles of enterovirus type 71 in different geographic regions > risk of introduction?

Van der Sanden et al., 2010
Key messages

● Food-borne virus transmission is common, but rarely diagnosed

● Substantial proportion relates to sewage contamination with multiple human and animal pathogens; sources of food (and sewage) global

● Toolbox for early detection depends on source of virus

● Nr of illness incidents overwhelms PH system, selection needed

● Internationally agreed criteria for detection needed

> risk based surveillance?
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Foodborne Viruses

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Saskia Rutjes
Martijn Bouwknecht

Food Borne Viruses in
Europe Network and global
noronet

www.noronet.nl