Public health risks associated with hepatitis E virus (HEV) as a food-borne pathogen

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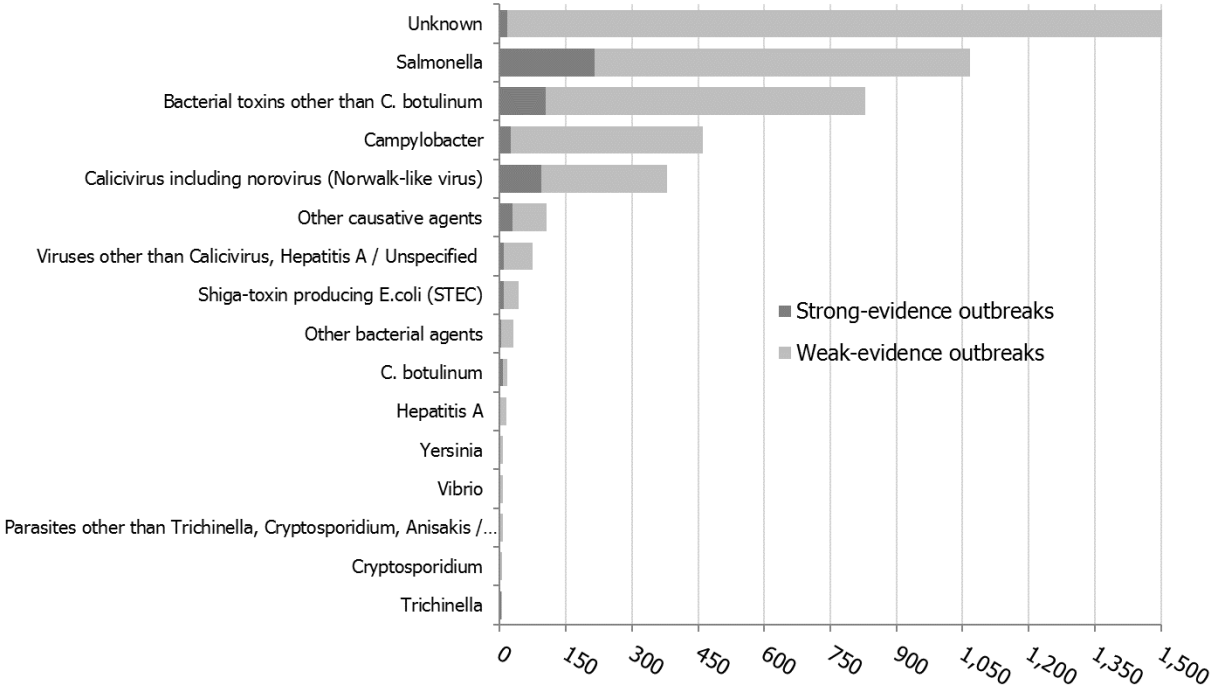
efsa
European Food Safety Authority

FBO surveillance data, EU, 2016

Distribution of strong-evidence and weak-evidence food-borne and waterborne outbreaks, per causative agent, EU, 2016



Other bacterial agents include *Francisella*, Enterococcus, Enterotoxigenic *E. coli* (ETEC), Enteroinvasive *E. coli* (EIEC), Enteropathogenic *E. coli* (EPEC), *Shigella* and other unspecified bacteria. Bacterial toxins other than *Clostridium botulinum* include toxins produced by *Bacillus*, *Clostridium* other than *Clostridium botulinum* and *Staphylococcus* and other unspecified bacterial toxins. Viruses other than Calicivirus and Hepatitis A include flavivirus, rotavirus and other unspecified viruses. Other causative agents include chemical agents, histamine, lectin, marine biotoxins, mushroom toxins, and scrombotoxin. Parasites other than *Trichinella* and *Cryptosporidium* include *Giardia* and other unspecified parasites

Reported FBO due to viruses, observations at EU-level

- 4,786 food-borne and waterborne OB have been reported in 2016 by 27 MS.
- **Viruses** ranked third causing **9.8% (N=470) of food- and water-borne OB** for which the causative agent was known, after bacterial agents (33.9% of all outbreaks) and bacterial toxins (17.7% of all OB).
- **At the EU level, no trends** in the OB reported were observed for Calicivirus and for viruses other than HAV and Calicivirus (adenovirus, flavivirus, rotavirus and other unspecified viruses), while for HAV, a mild reduction was observed in the 2010-2016 period.
- In terms of hospitalisations and deaths, OB caused by viruses presented the biggest health impact in the EU MS, after those caused by *Salmonella*. Calicivirus caused the **highest number of illnesses**, 11,993 cases (24.0% of all illnesses caused by all OB) and was associated with the highest mean number of cases per outbreak (31.6).

- Self-tasking mandate of the BIOHAZ Panel
- Update on 2011 opinion on foodborne viruses
- Adopted in June 2017

SCIENTIFIC OPINION

EFSA Journal

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Public health risks associated with hepatitis E virus (HEV) as a food-borne pathogen

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Abstract

Hepatitis E virus (HEV) is an important infection in humans in EU/EEA countries, and over the last 10 years more than 21,000 acute clinical cases with 28 fatalities have been notified with an overall 10-fold increase in reported HEV cases; the majority (80%) of cases were reported from France, Germany and the UK. However, as infection in humans is not notifiable in all Member States, and surveillance differs between countries, the number of reported cases is not comparable and the true number of cases would probably be higher. Food-borne transmission of HEV appears to be a major route in Europe; pigs and wild boars are the main source of HEV. Outbreaks and sporadic cases have been identified in immune-competent persons as well as in recognised risk groups such as those with pre-existing liver damage, immunosuppressive illness or receiving immunosuppressive treatments. The opinion reviews current methods for the detection, identification, characterisation and tracing of HEV in food-producing animals and foods, reviews literature on HEV reservoirs and food-borne pathways, examines information on the epidemiology of HEV and its occurrence and persistence in foods, and

Background

- HEV is most common cause of enteric viral hepatitis infection worldwide
- Most HEV infections are asymptomatic. However, HEV may be responsible for mild to fulminant acute hepatitis, and also chronic hepatitis in immuno-compromised patients
- Data on burden of HEV infections are limited due to the lack of surveillance in many EU countries

Terms of reference

1. To review methods for the detection, identification, characterisation and tracing of HEV, particularly assess their application to samples from FP animals and foods;

2. To review the literature on HEV reservoirs (human, animal and environmental) focusing on genotypes of public health significance;

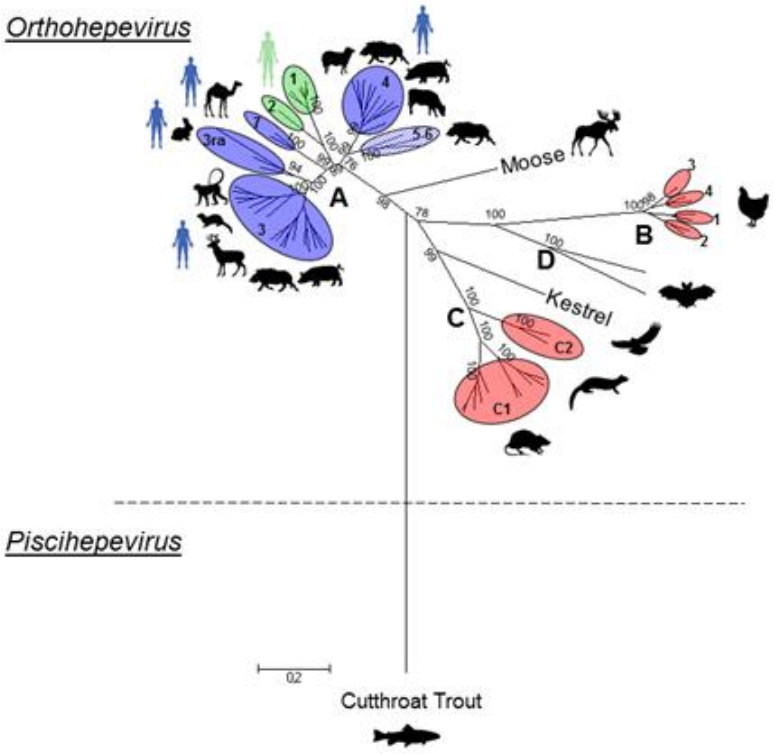
3. To examine information on the geographical distribution of HEV and epidemiology, occurrence and persistence in foods and consumer habits contributing to infection;

4. To investigate possible control measures along the food chain and evaluate decontamination treatments.

HEV genotypes

Orthohepevirus A

- 2 HEV genotypes (HEV-1 and HEV-2) found in humans only
- 2 genotypes (HEV-3 and HEV-4) found in both humans and animals. Associated with food-borne infections linked to pigs, wild boar and deer meat.
- Other closely related strains with more limited public health relevance found in a range of animals including wild boar (HEV-5 and HEV-6), rabbits (HEV-3ra) and camels (HEV-7 and HEV-8).



Methods

- Diversity of methods for HEV extraction and RNA purification from animals and food available. HEV Quantification protocols for HEV, based on several RT-PCR and LAMP techniques. Lacking standardisation and inter-laboratory validation.

- Several methods for subtyping of HEV strains for source attribution and tracing available. Recent definition of HEV subtype reference strains (WGS reference sequences for HEV-1 to HEV-7 subtypes proposed) and development of the web-based typing tool 'HEVnet' important steps towards harmonisation. Thresholds for definition of types, subtypes and 'identical' strains remain to be defined.

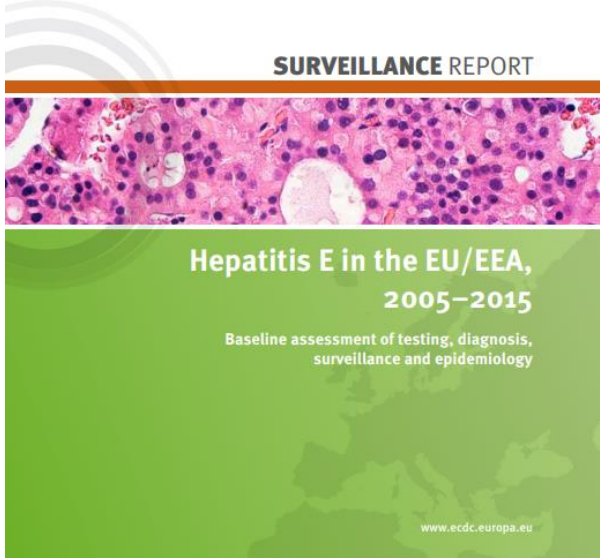
- Several tests available for detection of IgM or IgG in human and animal sera.

- Numerous descriptions of HEV isolation in cell culture exist, although isolation from low HEV concentration clinical samples is often unsuccessful

Surveillance

Hepatitis E virus is not notifiable at the European level, however notification requirement may be present in individual MS.

ECDC collected information about surveillance systems, case definitions and number of cases reported in MS.



Eurosurveillance, Volume 22, Issue 26, 29 June 2017

Surveillance and outbreak report

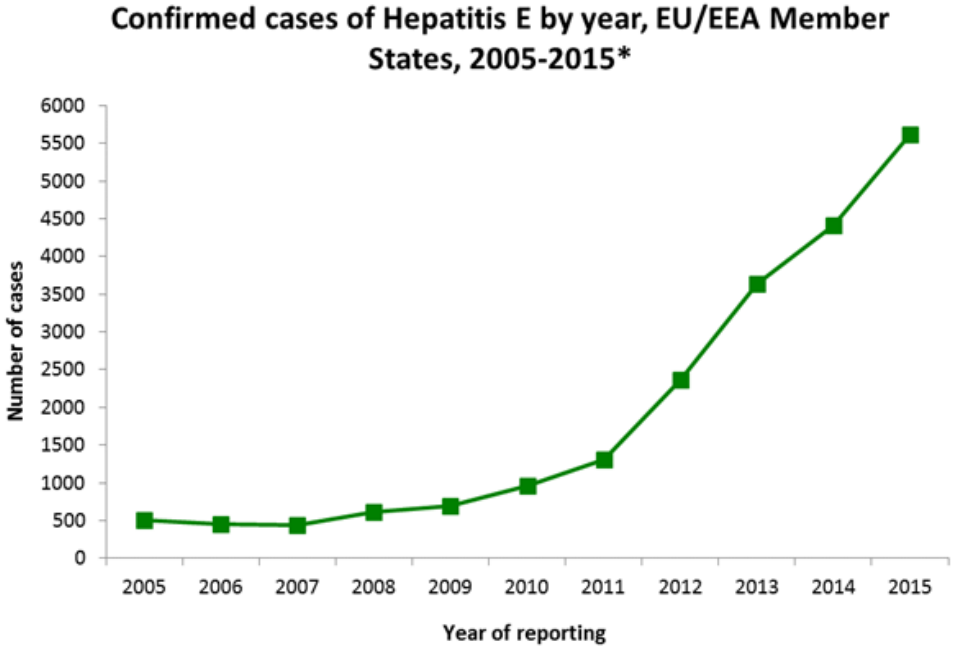
HEPATITIS E VIRUS INFECTION IN EUROPE: SURVEILLANCE AND DESCRIPTIVE EPIDEMIOLOGY OF CONFIRMED CASES, 2005 TO 2015

EJ Aspinall [1 2], E Couturier [3], M Faber [4], B Said [5], S Ijaz [5], L Tavoschi [6], J Takkinen [6], C Adlhoch [6], on behalf of the country experts [7]

HEV infection and disease in humans

- Hepatitis E is an important infection in humans in EU/EEA countries causing more than 21,000 mostly locally acquired reported clinical cases with 28 fatalities over the last 10 years with an increasing trend.
- Increase may be due to:
  - Greater awareness and increased testing
  - Switch in virus subtype observed in some EU/EEA countries
- >95% of human infections were autochthonous

Number of reported human HE cases by year from 22 EU/EEA countries ECDC, 2017)



HEV Transmission from FP animals and Food

- Food-borne transmission major pathway for human HEV infections in Europe.
- Raw or undercooked pork meat or pork liver sausages are the most frequently reported food products associated with sporadic cases or outbreaks of HEV.
- Prevalence of HEV in pig liver sausages: 10-29%
- Domestic pigs are the main animal reservoirs of HEV in the EU (27-94%). Wild boars are also an important reservoir (5-57%), but their population is lower compared to pigs and wild boar meat is less commonly consumed.
- Contact with infected animal reservoirs is also a risk for HEV. Personnel with professional occupation with pigs or wild boar are more frequently exposed than the general population.

HEV occurrence in animals

- **Pigs and wild boars** are the most important HEV reservoirs.
- HEV-infected pigs identified at the **farm and abattoir** in all countries where investigations have been carried out. HEV **prevalence** varies greatly, small non-industrialised production at higher risk in some studies.
- **Transmission** from infected sows to piglets, and trade in carrier pigs responsible for wide dissemination of infection.
- Specific **HEV strains** can persist for long periods on pig farms, a turnover of strains can also occur.
- HEV infection of pigs is largely subclinical, duration of **viraemia and faecal shedding** is variable. A proportion of pigs (less than 10%), remain viraemic at slaughter which results in some meat cuts containing HEV.
- Possible risk for **food cross-contamination** during slaughter, evisceration and food processing, including at home.
- HEV prevalence in **deer** is comparatively low.
- **Rabbits** appear to be resistant to infection with HEV-3 strains detected in humans and pigs.
- The zoonotic potential of HEV-7, HEV-8, and the risk of transmission from **camel** to humans remain to be elucidated.
- **Various animals**, such as moose, rats, ferrets, bats and several species of birds, can carry host-specific variants of HEV and there is currently no evidence for zoonotic transmission

HEV occurrence and persistence in food

- HEV has been reported in food of animal origin at slaughterhouse and point of sale. Products containing raw liver frequently found HEV-RNA-positive.
- HEV infection may be linked to consumption of raw or under-cooked virus-contaminated liver and processed meat products.
- Blood from viraemic animals could be a potential source of HEV infection if used in food products (e.g. blood sausages) that are insufficiently cooked.

HEV occurrence and persistence in food

- Other blood-derived products such as fibrinogen are increasingly used as ingredients and dietary supplements and may constitute a risk only if not properly heat-treated.

- The role of the environment (e.g. organic fertilisers or irrigation water) as source for HEV contamination of food of non-animal origin is unknown and should be evaluated.
- A small number of studies have reported a low prevalence of HEV in shellfish, soft fruit and vegetables.
- The virus could persist for several weeks in the environment. However, there are significant knowledge gaps

Control measures along food chain

- Control measures aimed to meat-borne parasitic or bacterial zoonoses are **not sufficient** to prevent HEV in pork.
- **Ante-mortem and post-mortem** inspection are **not able** to detect HEV.
- Some **farm management-based** methods (such as batching) can influence the time of first exposure to HEV, and there are **farm decontamination** measures for reduction of HEV risk in pig herds. These measures need to be confirmed in well-designed intervention studies.
- **Vaccination** of pigs is a potential control option, but its efficiency to prevent human disease requires further investigation. No vaccine is currently commercially available.
- Different combinations of **time-temperature** are effective in the inactivation of HEV-3, dependent on the used matrix. Boiling or stir-frying (internal temperature 71°C) for 5 min showed no residual infectivity in liver, whereas heating at 71°C for 20 min was necessary in pate-like preparations.
- Limited information is available on the effect of **biocidal treatments, disinfection and HPP** applied in the food industry on the infectivity of HEV. Radiation effectively reduce viral load within food, but this has not yet been investigated for HEV. Its use is restricted by EU legislation and by a lack of consumer acceptance.
- HEV is sensitive to current **water disinfection** treatments using chlorination and UV irradiation similar to other viruses. Various manure **composting and waste treatment** regimens have been shown to reduce environmental contamination by HEV, but wider studies analysing loss of HEV infectivity are required before firm recommendations can be made.

Control measures at consumer level

- There are several studies that identify consumption habits, consumption of raw or undercooked pork or wild boar products as risk factors for HEV infection in Europe.

- The development of validated quantitative and qualitative detection methods, including infectivity assays, and consensus molecular typing protocols is required for the development of quantitative microbial risk assessments and efficient control measures.

- In order to minimize the risk of an HEV infection, consumers should thoroughly cook especially pork and wild boar meat products. This recommendation applies in particular to especially vulnerable groups (e.g. persons with a weakened immune system, pre-existing liver injury).

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