

HEV2018

HEPATITIS E WORKSHOP

MADRID 4-5 JUNE 2018

**HEPATITIS E
PARADIGM OF A FOOD-BORNE
ZONOTIC EMERGING DISEASE IN EUROPE**

CONFERENCE HALL VISAVET CENTRE. UNIVERSIDAD COMPLUTENSE MADRID

Abstract book



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www.HEV2018.com



HEV2018 Hepatitis E Workshop Abstract book

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HEV2018 Hepatitis E Workshop

HEPATITIS E PARADIGM OF A FOOD-BORNE ZONOTIC EMERGING DISEASE IN EUROPE

**VISAVET Health Surveillance Centre. Universidad Complutense Madrid
4-5 June 2018. Madrid, Spain**

Abstract book



HEV2018 Committee welcome

Dear researches,

Welcome to Madrid and thanks for your participation in the **HEV2018 Hepatitis E: paradigm of a food-borne zoonotic emerging disease in Europe.**



Neglected and Emerging Diseases Unit of VISAVET-UCM organise this Med-Vet-Net workshop

The VISAVET centre of Complutense University of Madrid organize a Med-Vet-Net workshop focused on HEV by a One Health approach, connecting professionals from different expertise areas (clinicians, veterinarians, epidemiologists, food officers and policy makers) from different European countries.

The global workshop objective will be to share and update the knowledge about HEV at European level with the ultimate goal of establishing a hepatitis E consortium and a network in order to apply for European calls (Horizon 2020).

Hepatitis E virus (HEV) is an under-recognised cause of acute hepatitis in high-income countries. Originally considered to be restricted to humans, it is now clear that HEV and HEV-like viruses have several animal reservoirs with complex ecology and genetic diversity. Although there is a single serotype, four major HEV genotypes (1-4) capable of infecting humans are currently recognized. Genotype 3 predominates in high-income countries, including those in Europe. Transmission of this genotype is usually zoonotic and has been linked mainly to the consumption of pork products, but also to wild boar, deer or shellfish. EFSA has recently published a scientific report, which highlights a Europe-wide increase in cases and emphasizes the need for more research efforts on the epidemiology, diagnosis and control of HEV. Standardised case definitions and testing policies (including the development, harmonization and standardization of the detection methodology) would allow a better understanding of the epidemiology of HEV as an emerging cause of liver-related morbidity in Europe. Despite of major recent developments in the epidemiology, treatment, and prevention of hepatitis E, some other gaps in knowledge need to be addressed.

Nerea García-Benzaquén

Head of Organising Committee
HEV2018 Hepatitis E Workshop



Organisation





Organisers



Med-Vet-Net Association



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MADRID

VISAVET. Universidad Complutense Madrid

Organising and Scientific Committee

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- **Álvaro Fernandez-Manzano**
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VISAVET. Universidad Complutense Madrid. Spain.

Sponsor



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Med-Vet-Net Association

The **Med-Vet-Net Association** for Zoonoses Research was launched in October 2009 as a self-sustainable legacy of the Med-Vet Net NOE. Registered under French Law 1901 on 1 June 2009 with the primary objective of sustaining and common research activities, dissemination of scientific information, expertise and training and advocacy towards European stakeholders the Association is sustained by the contribution of an annual membership fee by each of its partner scientific Institutes.

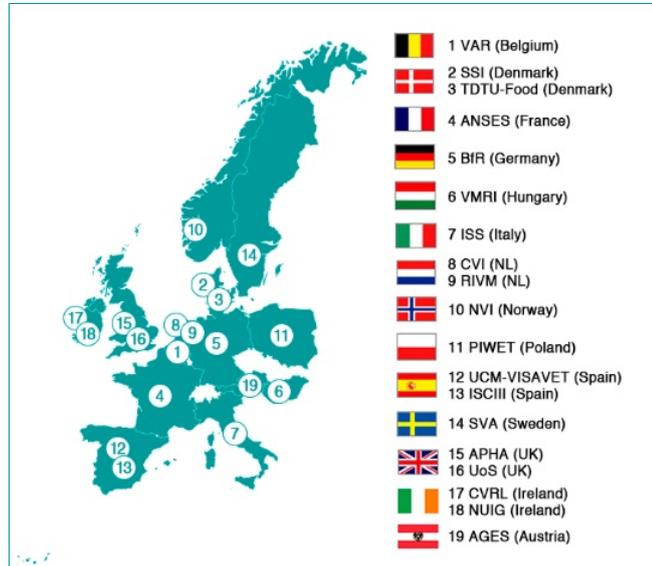


The association arose as a self-sustaining legacy of the highly successful Med-Vet-Net European Network of Excellence (NOE) for zoonoses research, which was initiated in September 2004 and funded for 5 years by the European Union (EU) 6th Framework Programme.

Established in response to the recognition of the enormity of the economic impact of zoonotic diseases and the requirement for better international, and national, level cooperation on animal and health issues, the Med-Vet-Net NoE developed a 'virtual institute' of multidisciplinary scientists. This brought together many of Europe's prominent research groups working on detection and control of zoonoses. The network comprised 14 science institute partners across Europe and over 300 scientists.

The partner institutes comprised eight veterinary, seven public health institutes from 10 European countries, including France, United Kingdom, Denmark, Germany, Hungary, Italy, Netherlands, Poland, Spain and Sweden. All partner institutes had national reference laboratory-based responsibilities for the prevention and control of zoonoses.

By adopting multinational and multidisciplinary approaches the work of veterinary, medical and food scientists, mainly in the field of food safety, was integrated at the European level, sharing knowledge to improve the prevention and control of zoonoses.



More info: <http://mvnassociation.org>



VISAVET-UCM

The **VISAVET Health Surveillance Centre** is a centre for research support and teaching belonging to the **Complutense University of Madrid** and is situated inside the complex to form with the Faculty of Veterinary Medicine and Veterinary Hospital.

The field work of VISAVET includes the following areas:

- Animal Health
- Public Health
- Food Safety
- Environment

The general aims of the Centre are Research and Training, together with technology transfer and activities of scientific and technical advice, within the areas mentioned above and aimed to the public and private sector.

To achieve these objectives, the VISAVET Centre:

- Participate and co-ordinate R&D projects
- Transfer the scientific advances to public and private sectors
- Advise companies and governments together with scientific and technological support
- Organize training courses and scientific and technical stays, for both students and professionals nationally and internationally
- Develop outreach activities to bring science closer to the society

VISAVET Centre has laboratories located in different areas of biological containment, designed and built to work with infectious agents at risk, in a completely safe for staff working in them and the community around them.

With a total area of 2000 m² has three distinct areas:

- Biosafety level 2 Area or BSL-2: It has laboratories and necropsy room specifically designed for the analysis of biological agents in Group 2.
- Biosafety level 3 Area or BSL-3: It has BSL-3 biosafety laboratories and BSL-3 necropsy room working with biological agents listed in Risk Group 3 (former OIE List A). This area has also a ABSL-3 animal facilities with three individual boxes with air conditioning and independent access to allow the simultaneous performance of different assays and controls.
- Cleanroom Area



VISAVET Central Units

- Project Management, Human Resources and Teaching Subdirection
- Quality and Biosafety Unit
- Clinical Trials Unit
- Information Technology and Communication Unit

VISAVET Research units

- Microbial Identification and Characterisation Unit
- Viral Immunology and Preventive Medicine Unit
- Mycobacteria Unit
- Pathology and Forensic Veterinary Medicine Unit
- Foodborne Zoonoses and Antimicrobial Resistance Unit
- Neglected and Emerging Diseases Unit

VISAVET Assistance

- Equine Health Surveillance Unit (SEVISEQ)
- Veterinary Livestock Assistance Unit (SEVEGAN)
- Madrid Emergency Veterinary Unit (SEVEMUR)

More info: <https://www.visavet.es>



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HEV2018

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Programme

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ZONOTIC EMERGING DISEASE
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ASSOCIATION

► EPIDEMIOLOG
AND PREVENTION
► P
► F
Abs
HEPATITIS E DIAGNOSIS
1.2 sub-genotype

PROGRAMME



Programme

Monday 4th June 2018

08:30 – 09:00 REGISTRATION

09:00 – 09:15 Welcome

Dr. María Teresa Gómez (Vice Dean of Research, Faculty of Veterinary Medicine. UCM, Spain)

Dr. Beatriz Romero (Deputy Director, VISAVET Centre. UCM, Spain)

Dr. Joaquín Goyache (Organising Committee, VISAVET. UCM, Spain)

09:15 – 09:30 Hepatitis E Workshop: a brief introduction

Dr. Nerea García (VISAVET. UCM, Spain)

09:30 – 10:00 Public health risks associated with hepatitis E virus (HEV) as a food-borne pathogen

Dr. Ernesto Liébana (EFSA, Italy)

HEPATITIS E EPIDEMIOLOGY

10:00 – 10:20 Hepatitis E in humans

Dr. Alfredo Pérez-Rivilla (H120, Spain)

10:20 – 11:10 COFFEE (& PHOTO)

11:10 – 11:35 Hepatitis E virus in animals, food and where else?

Dr. Nicole Pavo (ANSES, France)

11:35 – 11:50 Increasing trends of hepatitis E observed in hospital registries data, Spain 1997-2015

*Dr. Carmen Varela (ISCIII, Spain) *Selected oral presentation*

11:50 – 12:10 Transmission of hepatitis E virus at the wildlife-livestock- human interface

Dr. Jose Francisco Ruiz-Fons (IREC. CSIC-UCLM-JCCM, Spain)

12:10 – 12:35 Monitoring studies of food of animal origin in Poland - recent findings on HEV occurrence

Dr. Artur Rzezutka (NVI, Poland)



12:35 – 14:00 **LUNCH** (13:30 – 14:00 Optional visit to the VISAVET Centre)

HEPATITIS E DIAGNOSIS

14:00 – 14:15 **New proposed HEV-3 sub-genotype related to acute hepatitis in Spain**

*Dr. Ana Avellón (ISCIII, Spain) *Selected oral presentation*

14:15 – 14:40 **Detection and typing of the zoonotic Hepatitis E viruses**

Dr. Ilaria di Bartolo (ISS, Italy)

14:40 – 15:05 **Methods for analysis of HEV infectivity and inactivation**

Dr. Reimar Johne (BfR, Germany)

15:05 – 16:00 **COFFEE and POSTERS**

16:00 – 16:05 **Hepatitis E sponsor presentation**

Biomérieux S.A.

16:05 – 16:25 **Method comparison for the detection of Hepatitis E virus in lettuce and water samples**

Dr. Gloria Sánchez (IATA. CSIC, Spain)

16:25 – 16:55 **The communication challenge of infection diseases**

Dr. José Manuel Sánchez-Vizcaíno (VISAVET. UCM, Spain)

16:55 – 17:25 **Hepatitis E diagnosis and epidemiology table discussion**

20:00 **DINNER**

Tuesday 5th June 2018

HEPATITIS E CONTROL AND PREVENTION

09:00 – 09:20 **Inactivation of Hepatitis E virus: what we know and where we should go to**

Dr. David Rodríguez-Lázaro (UBU, Spain)

09:20 – 09:45 **The role of the environment in transmission of Hepatitis E virus**

Dr. Willemijn Lodder (RIVM, Netherlands)



09:45 – 10:00 **Investigating the transmission of Hepatitis E virus within a UK pig farm: Does early mixing affect risk of infection in slaughter age pigs?**

*Dr. Susan Withenshaw (APHA, UK) *Selected oral presentation*

10:00 – 10:25 **Hepatitis E virus control in the pig reservoir**

Dr. Wim van der Poel (WUR, Netherlands)

10:25 – 11:00 COFFEE and POSTERS

11:00 – 11:15 **Understanding hepatitis E virus (HEV) spread and persistence in pig farms using longitudinal field data**

*Dr. Morgane Salines (ANSES, France) *Selected oral presentation*

11:15 – 11:45 **Hepatitis-E in emergency context: the experience of Médecins Sans Frontières**

Dr. Francisco Luquero (MSF, Switzerland)

11:45 – 12:15 **Hepatitis E control and prevention table discussion**

12:15 – 12:30 **Closing of the meeting & Conclusions**

Dr. Nerea García (VISAVET. UCM, Spain)

Dr. Joaquín Goyache (VISAVET. UCM, Spain)

Dr. David Rodríguez-Lázaro (UBU, Spain)



HEV2018

HEPATITIS E WORKSHOP
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Awards





HEV2018 Med-Vet-Net Scholarships

The organization selected four communications among the received abstracts to grant them full cost scholarships (travel expenses, accommodation and attendance).

These communications were also selected for an oral presentation during the workshop.

To qualify for these scholarships there were two requirements:

- Present a communication abstract before the deadline
- Belong to a MedVetNet Association partner institution

1. Understanding hepatitis E virus (HEV) spread and persistence in pig farms using longitudinal field data
Dr. Morgane Salines (ANSES, France)
2. Increasing trends of hepatitis E observed in hospital registries data, Spain 1997-2015
Dr. Carmen Varela (ISCIII, Spain)
3. Investigating the transmission of Hepatitis E virus within a UK pig farm: Does early mixing affect risk of infection in slaughter age pigs?
Dr. Susan Withenshaw (APHA, UK)
4. New proposed HEV-3 sub-genotype related to acute hepatitis in Spain
Dr. Ana Avellón (ISCIII, Spain)





HEV2018 Med-Vet-Net Poster Award

A voting among the attendees was made to choose the best communication in poster format presented to the HEV2018 Hepatitis E Workshop.

After the recount of the results marked in the voting forms the awarded poster was:

Understanding hepatitis E virus (HEV) spread and persistence in pig farms using longitudinal field data

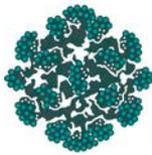
Dr. Morgane Salines (ANSES, France)





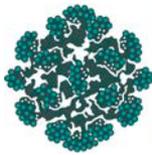
Oral Communications



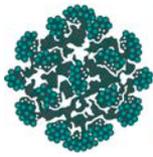


Oral communications

- S01. Hepatitis E Workshop: a brief introduction
Dr. Nerea García (VISA-VET. UCM, Spain)
- S02. Public health risks associated with hepatitis E virus (HEV) as a food-borne pathogen
Dr. Ernesto Liébana (EFSA, Italy)
- S03. Hepatitis E in humans
Dr. Alfredo Pérez-Rivilla (H120, Spain)
- S04. Hepatitis E virus in animals, food and where else?
Dr. Nicole Pavio (ANSES, France)
- S05. Increasing trends of hepatitis E observed in hospital registries data, Spain 1997-2015
*Dr. Carmen Varela (ISCIII, Spain) *Selected oral presentation*
- S06. Transmission of hepatitis E virus at the wildlife-livestock- human interface
Dr. Jose Francisco Ruiz-Fons (IREC. CSIC-UCLM-JCCM, Spain)
- S07. Monitoring studies of food of animal origin in Poland - recent findings on HEV occurrence
Dr. Artur Rzezutka (NVI, Poland)
- S08. New proposed HEV-3 sub-genotype related to acute hepatitis in Spain
*Dr. Ana Avellón (ISCIII, Spain) *Selected oral presentation*
- S09. Detection and typing of the zoonotic Hepatitis E viruses
Dr. Ilaria di Bartolo (ISS, Italy)
- S10. Methods for analysis of HEV infectivity and inactivation
Dr. Reimar Johne (BfR, Germany)
- S11. Method comparison for the detection of Hepatitis E virus in lettuce and water samples
Dr. Gloria Sánchez (IATA. CSIC, Spain)



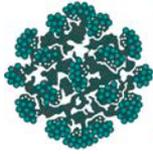
- S12. The communication challenge of infection diseases
Dr. José Manuel Sánchez-Vizcaíno (VISA-VET. UCM, Spain)
- S13. Inactivation of Hepatitis E virus: what we know and where we should go to
Dr. David Rodríguez-Lázaro (UBU, Spain)
- S14. The role of the environment in transmission of Hepatitis E virus
Dr. Willemijn Lodder (RIVM, Netherlands)
- S15. Investigating the transmission of Hepatitis E virus within a UK pig farm: Does early mixing affect risk of infection in slaughter age pigs?
*Dr. Susan Withenshaw (APHA, UK) *Selected oral presentation*
- S16. Hepatitis E virus control in the pig reservoir
Dr. Wim van der Poel (WUR, Netherlands)
- S17. Understanding hepatitis E virus (HEV) spread and persistence in pig farms using longitudinal field data
*Dr. Morgane Salines (ANSES, France) *Selected oral presentation*
- S18. Hepatitis-E in emergency context: the experience of Médecins Sans Frontières
Dr. Francisco Luquero (MSF, Switzerland)



García N. Hepatitis E Workshop: a brief introduction



García N. Hepatitis E Workshop: a brief introduction



Hepatitis E Workshop: a brief introduction

García N¹

¹NED Unit. VISAVET Health Surveillance Centre. Universidad Complutense Madrid, 28040 Madrid, Spain.

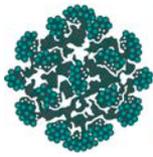
Hepatitis E virus (HEV) is an under-recognised cause of acute hepatitis in high-income countries. Originally considered to be restricted to humans, it is now clear that HEV and HEV-like viruses have several animal reservoirs with complex ecology and genetic diversity. Although there is a single serotype, four major HEV genotypes (1-4) capable of infecting humans are currently recognized. Genotypes 1 and 2 are restricted to humans, present in endemic areas where the virus is mainly transmitted through contaminated water. Genotype 3 predominates in high-income countries, including those in Europe. Transmission of this genotype has been mainly linked to the consumption of pork products, but also to wild boar, deer or shellfish.

EFSA and ECDC organisms had recently published scientific reports that highlights a Europe-wide increase in Hepatitis E cases and emphasizes the need for more research efforts on the epidemiology, diagnosis and control. Despite of major recent developments, some gaps in knowledge need to be addressed: true human and animal prevalence and incidence, effective infectivity methods, development of validated quantitative and qualitative detection techniques, harmonization of typing protocols, effective HEV control in meat production chains, refinement of treatment paradigms of acute and chronic hepatitis E, etc.

We present a workshop focused on HE by a One Health approach, connecting professionals from different expertise areas (clinicians, veterinarians, epidemiologists, food officers, policy makers, etc.) from different European countries. The structure of the Workshop consists in four coordinated thematic blocks (Introduction, Hepatitis E Epidemiology, Methodology and Control & Prevention) which covers the main aspects of the HE and HEV-infection.

The global workshop objective will be to share and update the knowledge about HE, mainly at European level, with the ultimate goal of establishing a hepatitis E consortium and a network in order to apply for European calls (Horizon 2020).

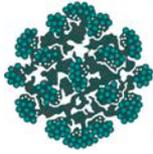
New advances in HEV knowledge should contribute to a better understanding of the epidemiology of this food-borne disease and the development of efficient prevention and control measures.



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



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



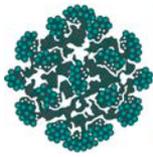
Public health risks associated with hepatitis E virus (HEV) as a food-borne pathogen

Liebana E¹

¹BIOCONTAM Unit. European Food Safety Authority, Parma, Italy

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 preexisting 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 investigates possible control measures along the food chain. Presently, the only efficient control option for HEV infection from consumption of meat, liver and products derived from animal reservoirs is sufficient heat treatment. 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. More research on the epidemiology and control of HEV in pig herds is required in order to minimise the proportion of pigs that remain viraemic or carry high levels of virus in intestinal contents at the time of slaughter. Consumption of raw pig, wild boar and deer meat products should be avoided.

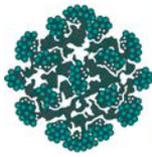
EFSA BIOHAZ Panel (EFSA Panel on Biological Hazards), Ricci A, Allende A, Bolton D, Chemaly M, Davies R, Fernandez Escamez PS, Herman L, Koutsoumanis K, Lindqvist R, Nørrung B, Robertson L, Ru G, Sanaa M, Simmons M, Skandamis P, Snary E, Speybroeck N, Ter Kuile B, Threlfall J, Wahlstrom H, Di Bartolo I, John R, Pavio N, Rutjes S, van der Poel W, Vasickova P, Hempen M, Messens W, Rizzi V, Latronico F and Girones R, 2017. Scientific Opinion on the public health risks associated with hepatitis E virus (HEV) as a food-borne pathogen. EFSA Journal 2017;15(7):4886, 89 pp. <https://doi.org/10.2903/j.efsa.2017.4886>



Pérez-Rivilla A. Hepatitis E in humans



Pérez-Rivilla A. Hepatitis E in humans



Hepatitis E in humans

[Pérez-Rivilla A¹](#)

¹Servicio de Microbiología. Hospital Universitario 12 de Octubre, 28041 Madrid. Spain

Hepatitis E virus (HEV) infection is the most common cause of acute viral hepatitis worldwide. Hepatitis E, until recently (mid-nineties) was exceptional in our environment and responsible for a minority of acute viral hepatitis related to travelling to endemic areas. However, the epidemiological information generated in the last 20 years, has revealed a new face of the HEV. Cases of locally acquired (autochthonous) hepatitis E have been reported throughout Europe, with no epidemiological history of travel to endemic areas.

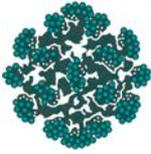
The hepatitis E virus is a heterogeneous group of viruses that infect a wide range of animal species. HEV genotypes responsible for most infections in humans are HEV1, HEV2, HEV3 and HEV4; but only one HEV serotype has been characterized, which may suggest that HEV antibodies (as those used in diagnostic tests) should be able to recognize different HEV strains.

Hepatitis E is a puzzling double-faced disease, with contrasting epidemiological and disease patterns in developing and developed countries. In developing countries, especially in Southeast Asia and Africa, HEV1 (rarest HEV2) are transmitted among humans (sole reservoir) mainly by faecal-oral routes, usually by contaminated water, with large outbreaks. It is usually an acute self-limiting illness, except in pregnant women and patients with underlying chronic liver diseases, who have high mortality rates. In contrast, autochthonous hepatitis E in Europe and most developed countries is mainly zoonotic, and the most prevalent genotype is HEV3. This genotype is transmitted mainly by direct contact with infected pigs, eating contaminated food products, or the environment. Patients are usually middle-aged/elderly males and a higher incidence of cases and severity in pregnant women has not been described. In addition, chronic HEV infection occurs in the immunosuppressed patients. From now on, I will focus on hepatitis E from developed countries caused by HEV3.

Anti-HEV IgG seroprevalence rates in Europe ranged from 0.6% to 52.5%. Considerable heterogeneity was found between studies, mainly attributable to the assay employed (vary considerably in sensitivity), the geographical location (between and within countries) and the type of study cohort (higher in individuals exposed to swine/wild animals). In addition, studies conducted before the year 2000, when performed with less sensitive first generation tests, led to the erroneous notion that HEV infection in Europe was rare and almost always imported from endemic developing countries. The HEV exposure rates observed in the seroprevalence studies, contrast with the relatively low number of hepatitis E cases reported in Europe.

Symptomatic HEV infection (majority are asymptomatic or unrecognised), occurs in 5-30% of individuals, indistinguishable from that caused by other hepatitis viruses and usually a self-limiting illness. Most autochthonous HEV disease occurs in older individuals and a minority of patients develop acute or subacute liver failure; such patients usually have underlying chronic liver disease. Chronic infection with HEV3 and HEV4 (viremia up to and beyond 3 mo) has been observed, most cases have occurred in solid-organ-transplant recipients; a few cases have been reported in individuals with haematological malignancies and patients with HIV/AIDS.

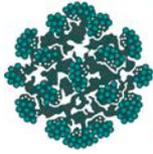
Because the infection is common and often asymptomatic, has raised concern of infection via blood donation. This risk may be significant in immunosuppressed patients or with chronic liver disease, as these patients often receive blood products.



Pavio N. Hepatitis E virus in animals, food and where else?



Pavio N. Hepatitis E virus in animals, food and where else?



Hepatitis E virus in animals, food and where else?

Pavio N¹

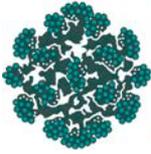
¹Animal Health Laboratory, French Agency for Food,
Environmental and Occupational Health & Safety (ANSES), 94700 Maisons-Alfort, France

The concept of zoonotic viral hepatitis E has emerged a decade ago following the discovery of animal strains of hepatitis E virus (HEV), closely-related to human HEV and with the description of autochthonous sporadic cases of hepatitis E in Western countries. Recent advances in the identification of animal reservoirs of HEV have confirmed that strains circulating in domestic and wild pigs are genetically related to strains identified in indigenous human cases. The demonstration of HEV contamination in the food chain or pork products has indicated that HEV is frequently a foodborne zoonotic pathogen. Direct contacts with infected animals, consumption of contaminated meat or meat products from suidae are all potential means of zoonotic HEV transmission. Other animal species, such as rabbit and camels harbour HEV related strains, more or less close to zoonotic strains and are possible reservoir for human contamination.

Until now, HEV screenings in food have focussed mainly on pork-derived meat and meat products. As suspected, several type of liver- meat pork products were found HEV positive (sausages, pies). However, it is possible that other food products such as meat or milk from other animal species (rabbit, camel), represent significant risks for zoonotic transmission of HEV. Other potential reservoirs such as ovine and bovine species are still debated. Further investigations are needed to screen for the presence of HEV RNA and infectious virus in larger variety of food products derived from various animal species.

HEV from infected human and animal faeces can be released in effluents (waste water treatment plants, slurry, organic fertiliser) leading to contamination of the environment. Hence, food of non-animal origin, such as crops, berries, and bivalve molluscs can be vehicles of HEV foodborne transmission. Since many of these products are consumed raw, they may cause constitute a public health risk. HEV RNA has been detected in irrigation water, raspberries and shellfish, indicating that HEV transmission may occur through secondary environmental contamination.

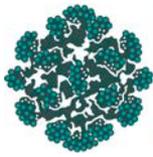
An exhaustive understanding of the extent of the animal reservoirs and transmission routes representing a risk for zoonotic hepatitis E infection is essential to prevent and control efficiently this disease in the future.



Varela C. Increasing trends of hepatitis E observed in hospital registries data, Spain 1997-2015



Varela C. Increasing trends of hepatitis E observed in hospital registries data, Spain 1997-2015



Increasing trends of hepatitis E observed in hospital registries data, Spain 1997-2015

Varela C^{1,2}, Martínez EV^{1,2}, Boix R^{1,2}, Avellón A³, Cano R^{1,2}

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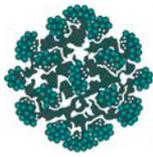
Hepatitis E is not included in the list of mandatory diseases under epidemiological surveillance; therefore the National Epidemiological Surveillance Network (RENAVE) would collect information only when an epidemic outbreak of hepatitis E occurs. However registries of hepatitis E hospitalized cases are available. The objective is to describe the epidemiological characteristics of hepatitis E cases in Spain with the available information.

A descriptive study was carried out, using data from the Basic Minimum Set of Data of Hospitalization (BMSD-H), from 1997 to 2015, that includes cases that have been at hospital at least for one night. Diagnoses were coded according to the International Classification of Diseases, 9th Revision, Clinical Modification. Diagnoses codes selected for the study were: 070.43 (hepatitis E with hepatic coma) and 070.53 (hepatitis E without mentioning hepatic coma). Moreover data from the outbreak system of the RENAVE from 2012 to 2017 was analysed.

Between 1997 and 2015 168 hepatitis E cases were registered at the BMSD-H. The median annual number of cases between 1997 and 2012 was three (range 1-12), number of cases was 26 in 2013, 27 in 2014 and 50 in 2015. Only 4 out of the 168 cases were under 15 years old, 43% of the cases belong to the 45-64 years old group. 128 of the cases were male and 40 were female (ratio male/female was 3.2). 9 deaths were reported among the registered cases: 6 were male and 3 female. Six of the death cases were older than 64 years old. No hepatitis E outbreaks were reported to the RENAVE.

Hospitalized hepatitis E cases have raised from 2013, being almost double in 2015 than in the two previous years. It may be due to some extent to an increase in awareness and testing. Cases were mainly adult males. There is not information related to risk factors or to no hospitalized cases. A pilot study to investigate the prevalence and risk factors of hepatitis E, together with a microbiological characterization, will contribute to the implementation of specific control measures.

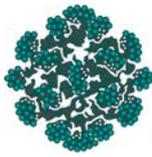




Ruiz-Fons F. Transmission of hepatitis E virus at the wildlife-livestock- human interface



Ruiz-Fons F. Transmission of hepatitis E virus at the wildlife-livestock- human interface



Transmission of hepatitis E virus at the wildlife-livestock- human interface

Ruiz-Fons F¹

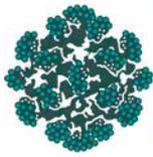
¹ Instituto de Investigación en Recursos Cinegéticos (CSIC-UCLM). 13071 Ciudad Real. Spain

Wildlife is at the origin of several of the most relevant human emerging diseases, e.g. SARS, MERS or Ebola, and it is also behind the emergence of high impact animal epizooties such as African swine fever in Europe. Transmission of multi-host pathogens shared by wildlife, livestock and humans occurs as a consequence of a complex interplay of factors leading to interactions between wildlife, livestock and humans at the wildlife-livestock-human interface (WLHI). The WLHI can be roughly defined from a health perspective as any interaction between wild and domestic (animals and humans) pathogen hosts leading to an effective inter-species transmission of a shared pathogen.

Hepatitis E virus (HEV) and HEV-like viruses have been identified in a wide range of wild species. Particular wild species are true reservoirs for specific HEV genotypes, e.g. wild boar for HEV-3, and transmit them to livestock and humans. Spill over hosts (non-maintenance reservoirs) may also be relevant actors for the maintenance of HEV at the WLHI if they are in close coexistence with true reservoirs, e.g. HEV-3 and HEV-4 in deer coexisting with wild boar. Currently HEV-3 and HEV-4 are the most relevant zoonotic HEV genotypes. Wild and domestic ungulates, rabbits and humans are the main actors in the life cycle of these genotypes. Human infections with other Orthohepevirus A viruses, e.g. HEV-7, have been reported only sporadically and there are no evidences of human infections by avian, rat, carnivore, bat or fish hepeviruses. There is also scarce evidence of wildlife-livestock transmission of avian, rat, carnivore, bat or fish hepeviruses.

How can hepeviruses be transmitted at the WLHI? Particular HEV genotypes shared by wildlife, livestock and humans, e.g. HEV-3 and HEV-4, are transmitted by the faecal-oral and food borne pathways. The contact with animals is a relevant driving factor for exposure to zoonotic HEV genotypes in humans. Neither indirect nor direct transmission routes at the WLHI have been proven for other wildlife hepeviruses. In industrialised countries transmission of zoonotic HEV genotypes from wildlife to humans occurs mainly as a consequence of exposure to animals and by the consumption of raw or undercooked game products. Transmission from wild to domestic animals may occur indirectly by contaminated food, e.g. pastures, and water. In non- industrialised countries food borne transmission through bushmeat should not be disregarded as a source for human infections.

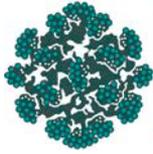
There are still too many gaps in knowledge on the ecology of wildlife hepeviruses that need to be properly addressed to inferring the potential risks they pose for livestock and human health. The patterns of wildlife-livestock-human interactions are changing worldwide as a consequence of human encroachment into wild ecosystems and human-induced environmental and climatic changes. Thereby, wildlife hepeviruses may emerge as livestock or human epizooties if given the chance to be transmitted at the WLHI.



Rzezutka A. Monitoring studies of food of animal origin in Poland - recent findings on HEV occurrence



Rzezutka A. Monitoring studies of food of animal origin in Poland - recent findings on HEV occurrence



Monitoring studies of food of animal origin in Poland - recent findings on HEV occurrence

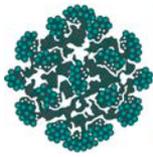
Rzeżutka A¹

¹ Department of Food and Environmental Virology, National Veterinary Research Institute, 57 Partyzantów Street, 24-100 Puławy, Poland

Hepatitis E virus (HEV) has been recognized as an emerging foodborne pathogen. After ingesting of contaminated food the virus usually produces a self-limiting hepatitis although in some patients serious health problems were also reported. Except HEV strains infecting solely humans, zoonotic or potentially zoonotic strains with no clinical significance for the host have been found in several species of food producing animals. Monitoring studies on HEV prevalence in ready-to-eat (RTE) pork meat products, slaughtered rabbits and edible snails entering food supply chain were conducted in Poland. RTE products representing two food categories such as raw meat products and variety of processed meat were subjected for virus testing. Pork liver and blood as incoming raw material used for food production were also tested. HEV was detected in 1.4% of tested food and raw material samples. It was present in black pudding and in sausage liver. Higher virus load than in RTE food was only found in pork blood. HEV RNA was not detected in pork liver, white sausage and onion spreadable sausage. Phylogenetic analysis of ORF 1 and ORF 2 virus sequences derived from pork blood indicated at subgenotype 3e virus strain. Except pork also rabbit or snail meat could be the virus source for humans especially when it is not sufficiently cooked. HEV RNA was solely found in one serum of slaughtered rabbit, although the presence of anti-HEV antibodies was shown in 7.8% sera. The detected rabbit HEV was closely related to other rabbit strains within genotype 3 HEV encompassing zoonotic virus strains. Similarly to tissues or meat of other animals intended for human consumption, snail meat should be free from microbiological hazards. During monitoring of farmed and free-living snails human enteric viruses including HEV were not detected in any of the tested snail samples. The overall microbiological status of snail meat indicated good hygiene and appropriate environmental conditions maintained during snail breeding. Only the soil samples from the plots used at the fattening stage were characterised by a high microbial content increasing the risk of virus occurrence.

Pork and rabbit meat containing HEV could enter the food chain. In addition, HEV detection in RTE pork products indicates insufficient thermal processing of food. Nevertheless, sporadic HEV detection and low virus concentration in these food type indicate that the risk of infection associated with their consumption could be considered negligible. A negligible risk of infection is also associated with farm-raised snails, although consumption of wild-type snails increases this risk.

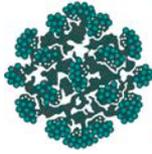
Studies were funded by the KNOW (Leading National Research Centre) Scientific Consortium "Healthy Animal – Safe Food", under Ministry of Science and Higher Education decision No. 05-1/KNOW2/2015 and research project no. S/198.



Avellón A. New proposed HEV-3 sub-genotype related to acute hepatitis in Spain



Avellón A. New proposed HEV-3 sub-genotype related to acute hepatitis in Spain



New proposed HEV-3 sub-genotype related to acute hepatitis in Spain

Avellón A¹, Muñoz-Chimeno M¹, Arroyo S¹, Morago L¹, Molina AA¹

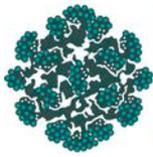
¹Hepatitis Unit. Viral Hepatitis Reference and Research Laboratory. National Center of Microbiology. Carlos III Health Institute. Madrid. Spain

Hepatitis E virus (HEV) genotype 3 (HEV-3), is responsible for most HEV infections in Europe, and shows an increasing incidence in the continent. Sub-genotypes (SG) from 3a to 3j were firstly defined and used for epidemiological purposes on the basis of genome partial sequences. Consideration of just two genetic groups (3jab/3chi and 3feg) was after proposed. However, the former SG classification is still in use and was applied to describe the temporal evolution of the virus in France and to describe the proposal of reference sequences for each SG (Smith et al., 2016). In 2017, novel proposed HEV-3 SGs have been described in Japan and China on the basis of complete genome analysis. The aim of this study is characterize a new proposed HEV-3 SG which has been associated to acute hepatitis in Spain.

From the analysis of SG distribution in Spain (of 93 HEV-3 ORF2 sequences from 2009 to 2016), seven sequences did not grouped with any of the proposed reference sequences. This study consist on obtaining the complete genome sequence of one of them (Id. KU513561-Spain) by means of Sanger sequencing and assessing phylogenetic analysis results (ML tree and p-distance, Mega 7.0) after being compared to HEV reference sequences and all complete HEV sequences available in Genbank database.

P-distance among SG reference sequences ranged from 0.119 to 0.181. A Maximun Likely-hood tree was built, and according to sequence clustering with the reference sequences and a p-distance less 0.115, SGs where assigned. Among the unassigned sequences, KU513561-Spain was close to KU176130-France. Both sequences had a p-distance 0.130 or higher after being compared with any other sequence in the tree suggesting the possibility of a new SG. This p-distance was in similar range of the new recently proposed SGs in Japan and China. Ministry of Science and Higher Education decision No. 05-1/KNOW2/2015 and research project no. S/198.

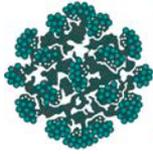




Di Bartolo I. Detection and typing of the zoonotic Hepatitis E viruses



Di Bartolo I. Detection and typing of the zoonotic Hepatitis E viruses

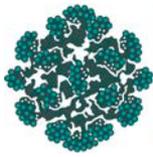


Detection and typing of the zoonotic Hepatitis E viruses

Di Bartolo I¹

¹ Department of Food Safety, Nutrition and Veterinary Public Health.
Unit of Emerging Zoonoses. Istituto Superiore di Sanità, 00162 Rome. Italy

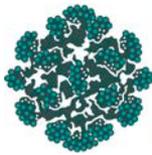
Hepatitis E virus is quasi-enveloped virus, with a single strand positive RNA genome. The viral genome (ssRNA) is structured in short 5' and 3' untranslated regions (UTR) and three Open Reading Frames (ORF1, ORF2 and ORF3) encoding, the non-structural proteins, the capsid protein and a small multifunctional phosphoprotein, respectively. The virus has recently been classified in the family of Hepeviridae, including 2 species: Piscihepevirus and Orthohepevirus. The former includes strains infecting cutthroat trout and the latter, several mammalian species as well as avian. Orthohepevirus includes 4 species and most of the viral strains identified so far. Orthohepevirus B, C and D strains infect avian species, bats, rats and other mammals, and have not been identified in humans. Orthohepevirus A includes strains infecting humans, pigs, wild boar, deer, mongooses, rabbits and camels, which are classified into 7 genotypes (HEV1-7) with an additional proposed genotype 8 recently detected in Bactrian camels. The genotypes are divided into subtypes based on comparisons of HEV complete genome sequences. A novel subtype can be established if at least three genomes from epidemiologically unrelated strains are available that form a cluster of related viruses which is divergent from existing subtypes. However, up to date a cut off value to distinguish subtypes has not been defined yet. Over the last few years, novel subtypes have been proposed for HEV strains with sequences that share a limited nucleotide identity (<85-87%) with other sequences available online. These strains do not belong to previously defined subtypes. Some other subtypes include strains that rarely circulate. The biological meaning of the subtypes has not been proved yet; it may somehow be correlated to virulence. However, classification of genotypes in subtypes is useful for the monitoring of evolutive changes of the circulating strains and helpful for diagnoses. Indeed, up to date laboratory techniques for direct and indirect diagnostics do not allow for a distinction between the different genotypes or subtypes. Several methods to extract HEV RNA by biological matrices (animal or non-animal origin) and environmental samples, have been used in studies for the detection of HEV. However, some of them showed a limited sensitivity and results obtained among different studies are not always comparable. A standardized method for RNA detection and quantification is needed to harmonize results.



Johne R. Methods for analysis of HEV infectivity and inactivation



Johne R. Methods for analysis of HEV infectivity and inactivation



Methods for analysis of HEV infectivity and inactivation

Johne R¹

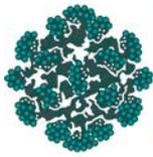
¹ Department Biological Safety, Food Hygiene and Virology,
German Federal Institute for Risk Assessment, 10589 Berlin, Germany

Detection of HEV is currently mainly done using molecular techniques like real-time RT-PCR. Although these methods represent specific and sensitive techniques for the detection of the HEV genome, they cannot distinguish between infectious and inactivated virus. However, a measurement of the HEV infectivity is crucial for assessing the risk of infection originating from specific food products and estimation of the HEV inactivation by food processing or disinfection procedures.

HEV infectivity determination is still hampered by the lack of efficient and robust experimental systems. Limited studies on HEV inactivation have been done by experimental inoculation into pigs followed by monitoring seroconversion and virus shedding. By this, first data on heat stability of HEV in selected food products could be generated. However, the applicability of this system is restricted due to its limited possibility of experimental repetition, unsuitability for performing large numbers of tests, high costs, and not least ethical considerations.

The use of cell culture systems may overcome these problems, but descriptions of robust and sensitive systems for use in HEV inactivation studies are rare. We attempted to isolate efficiently replicating HEV strains by inoculation of samples from HEV-infected wild boars and humans onto the human lung carcinoma cell line A549. Only one strain, derived from a chronically HEV-infected patient and designated as strain 47832c, showed efficient and reproducible growth. The strain is of genotype 3c and contains an unusual insertion within its ORF1-encoding hypervariable region. Further optimization of the system was done by establishing subclonal cell lines. One of these cell lines, designated as A549/D3, showed a higher susceptibility and faster virus growth as compared to the parent cell line. Although the optimized cell culture system allows the titration of HEV infectivity within a 4 log₁₀ range, it still requires more than 3 weeks for infectivity testing. The cell culture system was used to assess the HEV long-term stability and influence of short term heating in cell culture medium. Remaining HEV infectivity could be demonstrated after 1 month storage at room temperature and after 2 months at 4°C. Heating for 1 min up to 60°C only slightly decreased the virus titer, whereas no remaining virus could be detected after 1 min heating at 80°C. The data were used for development of a model, which can predict the HEV inactivation at a distinct time/temperature combination.

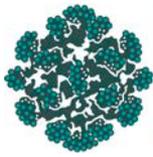
Studies on meat products artificially contaminated with HEV strain 47832c are planned in order to analyse the HEV stability during sausage production. The establishment of efficient virus extraction methods from meat products was identified as a crucial step, which is currently optimized. The system shall be applied in future to investigate the infectivity of HEV in distinct meat products and to assess the efficiency of HEV inactivation during food processing and disinfection. Alternative methods like capsid stability assays and viability PCR techniques may be developed and compared with the cell culture system in order to provide rapid and easy-to-perform methods for HEV infectivity estimation in the future.



Sánchez G. Method comparison for the detection of Hepatitis E virus in lettuce and water samples



Sánchez G. Method comparison for the detection of Hepatitis E virus in lettuce and water samples



Method comparison for the detection of Hepatitis E virus in lettuce and water samples

Sánchez G¹, Randazzo W^{1,2}, Vasquez-García A³, Bracho MA^{4,5}, Alcaraz MJ⁶, Aznar R^{1,2}

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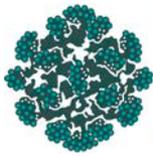
³Faculty of Animal Science and Food Engineering, University of São Paulo. 13635-900 Pirassununga, Brazil.

⁴Microbiology Service, Hospital Clínico Universitario. 46010, Valencia, Spain.

⁵Joint Research Unit in Infection and Public Health, FISABIO-Public Health – University of Valencia. 46020. Valencia, Spain.

⁶CIBER Epidemiología y Salud Pública, Valencia, Spain

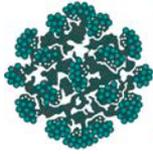
Hepatitis E virus (HEV) is a zoonotic pathogen that causes acute hepatitis which in some cases may progress to chronic hepatitis. The main transmission routes of HEV are contaminated water, consumption of raw or undercooked meat from pigs or wild boar, blood transfusion, and organ transplantation. However, patients suffering from hepatitis E may excrete up to 10¹¹ genome copies per gram of feces prior to being symptomatic; therefore, infection can also occur through the fecal–oral route either by direct contact with an HEV-infected person or by ingestion of contaminated food or water. Although the role of HEV transmission through contaminated produce has not been confirmed, the presence of HEV has been reported in irrigation waters and in vegetables. The present study used a WHO international standard and Spanish clinical samples to evaluate the performance characteristics of three RT-qPCR assays for detection and quantification of HEV. Two of the evaluated assays provided good analytical sensitivity, as 250 international units (IU)/ml could be detected. Then, experiments focused on evaluating the elution conditions suitable for HEV release from vegetables, with the method proposed by the ISO 15216:2017 selected for evaluation in three types of fresh vegetables. The concentration method proposed by the ISO 15216:2017 combined with the RT-qPCR described by Schlosser et al. (2014) resulted in average HEV recoveries of 1.29%, 0.46%, and 3.95% in lettuce, spinach, and pepper, respectively, with an average detection limit of 1.47 × 10⁵ IU/25 g. In naturally contaminated samples, HEV was detected in sewage only (14/57), while no detection was reported in lettuce (0/36) or in irrigation water samples (0/28). Finally, to enable differentiating between infectious and inactivated viral particles, different pretreatment of nucleic acid with intercalating dyes were evaluated.



Sánchez-Vizcaíno JM. The communication challenge of infection diseases



Sánchez-Vizcaíno JM. The communication challenge of infection diseases



The communication challenge of infection diseases

Sánchez-Vizcaino JM¹

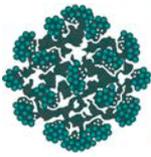
¹SUAT Unit. VISAVET Health Surveillance Centre. Universidad Complutense Madrid, 28040 Madrid, Spain.

In the world of information, immediacy is a value that often is weighted more than any other. Today, the rise of social networks has become immediate means, a facet seated in the world of information, and it is necessary to think about what role the emitters in the food and health crises have to play, among which have a natural tendency to generate alarms.

The information sources should be aware of this reality and be prepared for it, to avoid that an appearance of a crisis becomes, by a bad communication, in a real problem. We must not forget that no decisive battle of the contemporaneity can escape out of the media. However, it occurs with some frequency that health crises maximum match the expectation, and is the moment in which the media devote more space to the novelty -the news, by definition, is novelty- with the greatest difficulty to provide truthful and evidence-based information from the sources.

The lack of information brings us to the disinformation, to the concerned speculation, and to the emergence of emotional elements in the transmission of information. This globalisation of information and the technological development of the media - broadcast in real time, fragmentation of audiences, personalization and interactivity of the messages, the ability of the receivers to become massive emitters, etc.- are revolutionizing the social communication, and the communication in crisis situations, in particular the health ones. We face an increasingly complex scenario in which the proper relationship between the media and the institutions have a fundamental role.

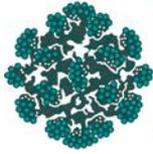
This lecture focuses on a summary of risk infectious diseases communication experiences lived among the years and tries to establish a comparison with the HEV, and concludes that this virus has not risk perception among the general population of a large number of European countries, despite increasing its detection in the last years. The reasons why it happen will be analyzed.



Rodríguez-Lázaro D. Inactivation of Hepatitis E virus: what we know and where we should go to



Rodríguez-Lázaro D. Inactivation of Hepatitis E virus: what we know and where we should go to



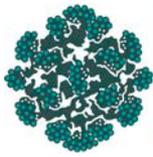
Inactivation of Hepatitis E virus: what we know and where we should go to

Rodríguez-Lazaro D¹

¹ Microbiology Division. Department of Biotechnology and Food Science.
University of Burgos, Burgos, Spain

Several cases of foodborne transmission of hepatitis E have been reported, often involving consumption of meat, especially raw or undercooked. Although information is lacking on the exact extent of foodborne transmission of hepatitis E virus (HEV), effective methodology for its inactivation is a growing demand for and from the Food Industry and food policy makers. There are significant gaps in our knowledge regarding the survival of HEV in foods and the environment (including food contact surfaces), and also regarding the effect of elimination procedures used in food supply chain settings. There has been a very limited range of studies on the heat resistance of HEV, but the information from has raised questions regarding what may be the most effective cooking procedure to inactivate the virus.

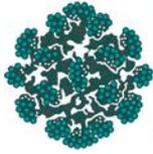
The lack of a reliable infectivity assay has hampered extensive study. It has been recommended that studies be undertaken to develop an efficient propagation system (based on in vitro cell culture), to facilitate the acquisition of extensive information on the potential risk posed by of HEV foodstuffs and the environment, and its response to disinfection and elimination procedures. In addition, non-standardised protocols for the accurate detection HEV from food products have been developed. This lack of harmonization implies that the diverse studies have used different detection methodologies, and consequently the results obtained in those studies cannot be compared easily. However, it is essential that alternative (non-thermal) inactivation methodologies are explored to guarantee Food Safety Objectives (FSO) for this virus.



Lodder W. The role of the environment in transmission of Hepatitis E virus



Lodder W. The role of the environment in transmission of Hepatitis E virus



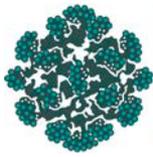
The role of the environment in transmission of Hepatitis E virus

Lodder W¹

¹ National Institute for Public Health and the Environment, RIVM, Netherlands

Non-travel-related hepatitis E virus (HEV) genotype 3 infections in persons in developed countries have a zoonotic origin. Because domestic pigs, wild boar and deer are considered the prime reservoir, transmission through consumption of contaminated pork, wild boar or deer products is suspected, but there are indications that environmental transmission may contribute to human disease cases as well. The attribution of these possible environmental transmission routes to exposure and infection of HEV is unknown. When more is known on the attribution of environmental transmission, cost-effective preventive actions can be taken to reduce exposure to HEV through the transmission routes concerned, such as treatment of wastewater and manure, using clean irrigation water, use treated fertilizers and apply appropriate hygiene measures. In addition, reduction of HEV exposure may be obtained by advising (vulnerable) populations to avoid consumption of food products that may contain HEV.

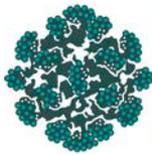
Thus, although the omniprevalence of HEV in the environment has been demonstrated, most studies on transmission focus on the consumption of pig or pig products. At present, little information on the attribution of environmental transmission routes to the disease burden of HEV is available. This information is indispensable to decide which intervention measures are most (cost) effective and should get more focus in future research programs.



Withenshaw S. Investigating the transmission of Hepatitis E virus within a UK pig farm



Withenshaw S. Investigating the transmission of Hepatitis E virus within a UK pig farm



Investigating the transmission of Hepatitis E virus within a UK pig farm: Does early mixing affect risk of infection in slaughter age pigs?

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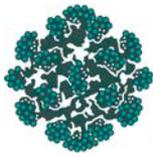
²Department of Virology, Animal and Plant Health Agency, Addlestone, UK

The incidence of non-travel related human Hepatitis E (HEV) infections in the UK has been increasing in recent years, as in many countries, thus suggesting an emerging route of infection via the consumption of infected pork. HEV infection in UK pig herds is believed to be widespread, and although UK-produced pigs currently appear to be infected with different HEV strains to those involved in most human cases in the UK, the consumption of infected UK-produced pork could emerge as a route of human infection in future. It is therefore necessary to understand what factors determine HEV infection in pigs at slaughter, so that control strategies can be developed to minimise this risk.

In a recent abattoir study, a high prevalence of HEV antibodies were detected in pigs at slaughter (92.8%), suggesting that pigs' exposure to HEV infection at some point during production is common. However, prevalence of detectable active infection (viraemia) was much lower. A subsequent risk factor analysis using this dataset found that pigs from finisher farms were less likely to be viraemic at slaughter if they had been present on the farm from an earlier age (i.e. arrived as growers) compared to pigs that had arrived at a later age (i.e. as finishers). This circumstantial evidence suggests that mixing groups of pigs together at an earlier age (and therefore providing opportunities for HEV transmission and subsequent recovery) may reduce the risk of pigs remaining viraemic at slaughter, possibly as earlier infection facilitates greater herd immunity at slaughter age. Here we present details of a current study of HEV transmission on an indoor farrow-to-finish farm in the UK where we are investigating this hypothesis.

We are tracking a cohort of pigs from pre-weaning to finisher age to determine how presence of infection changes in the group as it progresses through different stages of production. Infection status is determined through collection of faeces, and presence of viral shedding is used as an indirect measure of infection status. The cohort is divided across a number of pens at each production stage, and we will determine the presence of infection at the pen-level, and prevalence of infection across each production stage. Crucially, pigs from different pens are mixed together at different stages of production, and different pigs may experience mixing at different ages. By keeping detailed records of how groups of pigs are mixed together, we therefore aim to identify whether the timing and frequency of group mixing within the study cohort affects the presence of infection at slaughter age.

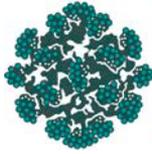




Van der Poel WHM. Hepatitis E virus control in the pig reservoir



Van der Poel WHM. Hepatitis E virus control in the pig reservoir



Hepatitis E virus control in the pig reservoir

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¹Wageningen Bioveterinary Research, Lelystad, The Netherlands

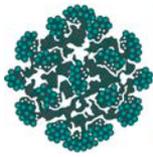
Hepatitis E virus (HEV), genotypes 3 and 4 have zoonotic potential and cause single cases of hepatitis throughout the world. Both of these genotypes have a main reservoir in domestic swine and this leads to contaminations in the food chain. The virus may be transmitted to humans by different types of foods including meat products, and as environmental routes may be involved, also water, shellfish, fruits and vegetables.

HEV is a relatively stable non-enveloped virus, and may remain infectious at temperatures used in some cooking regimes. Best feasible inactivation methods include heating at plus 71C, chlorine treatment and UV light. Focal points for control along the food chain depend on the type of food and the stage in the food production process.

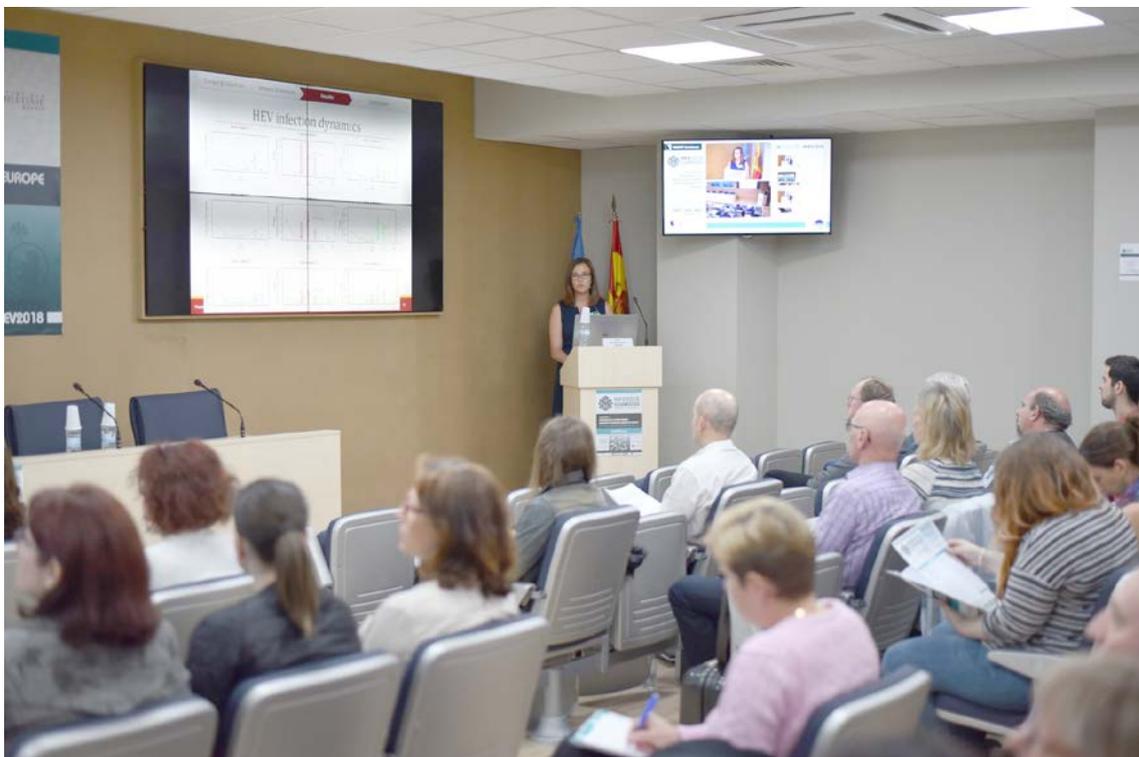
Besides control options at the pork retail level and by the consumer it is important to try to reduce HEV in primary production and the whole swine reservoir. (FSA-EFSA stakeholder meeting, 2018). Raising the level of biosecurity on swine farms is indicated, so farms should review and tighten their biosecurity protocols and be especially diligent about visitors and supplies, feed ingredients, food items, etc. However, there is a lack of knowledge on sources of HEV introduction in swine farms and on HEV dynamics and transmission between and within farms. Such information will be needed to further improve effective control and prevention strategies.

Effectively reducing the HEV prevalence in the animal reservoir by bringing biosecurity on a higher level may prove to be very difficult. To reduce the fraction of infectious animals at slaughter age and thus the risk for public health, a vaccination programme may be needed. However, in Europe a HEV vaccine still has to be brought to market. In case such a vaccine is unable to eliminate the virus, it needs to be taken into account that a shorter mean infectious period decreases the fraction of infectious animals at slaughter age, whereas a reduced transmission rate parameter adversely increases it. With a reduced susceptibility, vaccination of animals at a later age can be a better strategy than early vaccination.

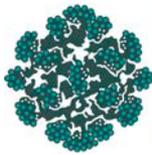
Currently there is a fear that the number of HEV infections in immunocompromised patients may increase and that we may see more extrahepatic manifestations of HEV infection in future. This emphasizes the need for more study on prevention and control of HEVs for improvement of food safety and public health protection.



Salines M. Understanding HEV spread and persistence in pig farms using longitudinal field data



Salines M. Understanding HEV spread and persistence in pig farms using longitudinal field data



Understanding hepatitis E virus (HEV) spread and persistence in pig farms using longitudinal field data

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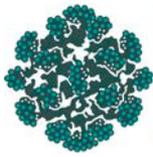
Hepatitis E virus (HEV) is a zoonotic pathogen mainly transmitted through the consumption of contaminated pork products. This study aimed at describing HEV infection patterns in pig farms and at assessing the impact of factors related to intercurrent viral co-infections, HEV immunity status and litters' characteristics on HEV dynamics in field conditions. According to previous experimental results showing strong interactions between Porcine Reproductive and Respiratory Syndrome virus (PRRSv) and HEV, the focus was made on immunomodulating pathogens frequently encountered in pig farms (PRRSv and Porcine Circovirus type 2, PCV2).

A longitudinal follow-up was conducted in three HEV-infected farrow-to-finish farms. Forty piglets in three batches per farm were randomly sampled and individually monitored from birth to slaughter. Blood and faecal samples were taken at 1, 6, 10, 14, 18 and 22 weeks of age; blood and liver samples were collected at slaughterhouse. Virological and serological analyses were performed to assess HEV, PCV2 and PRRSv infection dynamics. The links between 12 explanatory variables and four outcomes describing HEV dynamics were explored using survival analysis and logistic regression considering within-farm piglets' clustering.

HEV infection dynamics was highly variable between farms and in a lower magnitude between batches. HEV positive livers were more likely related to short time-intervals between HEV infection and slaughter (OR=4.07 [3.72-4.45]). In addition to an influence of piglets' sex and sows' parity, the sequence of co-infections strongly affected HEV dynamics. Prior or concomitant infection by PRRSv or PCV2/PRRSv significantly delayed the age at HEV shedding (Hazard Ratio = 0.28 [0.17-0.47], HR=0.26 [0.15-0.46], respectively). The age at HEV seroconversion was delayed (HR=0.43 [0.25-0.74]) in PCV2/PRRSv co-infected piglets, also showing a delayed end of HEV shedding (HR=0.50 [0.32-0.79]) which resulted in a longer shedding period in those co-infected piglets. Consequently, a PRRSv or PCV2/PRRSv pre- or co-infection dramatically increased the risk of positive livers at slaughter (OR=4.10 [1.87-8.97], OR=6.49 [3.18-13.23], respectively).

Co-infections with immunosuppressive viruses, mainly PRRSv or associations between PRRSv and PCV2, affected HEV dynamics. Controlling these pathogens may be a major lever to mitigate the risk of having long term shedding of HEV leading to contaminated carcasses at slaughter entering the food chain. It demonstrates the need for a more global approach including the control of pathogens involved in pig health to minimize the risk of exposure to this zoonotic virus.

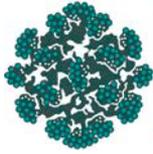




Luquero F. Hepatitis-E in emergency context: the experience of Médecins Sans Frontières



Luquero F. Hepatitis-E in emergency context: the experience of Médecins Sans Frontières



Hepatitis-E in emergency context: the experience of Médecins Sans Frontières

Luquero F¹

¹Médecins Sans Frontières. MSF. Switzerland

Médecins Sans Frontières (MSF) has supported several Ministries of Health to fight large hepatitis E outbreaks, many of them taking place in areas of conflict among displaced populations. Despite the increase attention that hepatitis E is receiving in developed countries, the heaviest burden of diseases remains in countries located in Asia and Africa where hepatitis E is endemic and the virus cause large outbreaks. Nonetheless, the weakens of the surveillance systems in this countries is likely biasing down the true burden of diseases; which is disproportionally higher among pregnant women, especially among those in the third trimester where the case fatality risk can be as high as 25% along with an increased risk of stillbirths.

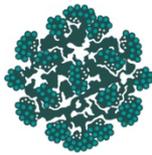
The difficulties in managing acute liver failure in the contexts where these outbreaks occur along with a lack of effective therapies makes these protracted outbreaks difficult to manage and control. Hepatitis E is considered a waterborne disease in endemic areas of Asia and Africa and thus improvement in access to safe water and sanitation and hygiene will be required to achieve control. However, there is a general agreement that this improvements, which are truly needed, will be difficult to achieve in the short term. In addition, emergency water and sanitation interventions have proven to be insufficient to control epidemics. A new safe and highly efficacious vaccine licensed in China in 2011 could complement the available tools to prevent the diseases. However, despite the WHO recommendation of using the vaccine in response to outbreak, the lack of prequalification together with a non-adapted vaccine presentation with 3-dose schedule is limiting its used in the field.

This presentation will include several examples from Niger, Chad, Sudan and Nigeria illustrating the above mentioned challenges to fight large outbreak in the field as well element of discussion to achieve improvements including areas for further research



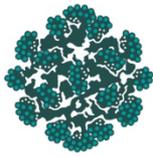
Poster communications



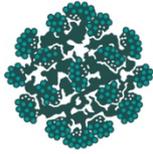


Poster communications

- P01. Swine and wild boars as potential zoonotic reservoir of hepatitis E in Romania
Aniță AE (University of Agricultural Sciences and Veterinary Medicine, Romania)
- P02. Risks, burden and socio-biology of hepatitis E infection in England
Vaughan A (Public Health England, UK)
- P03. Use of liver transudation as an alternative matrix for the diagnosis of Hepatitis E using a commercial ELISA kit
Navarro A (Universidad Complutense Madrid, Spain)
- P05. Human hepatitis E in Romania: autochthonous or/and imported?
Porea D (University of Agricultural Sciences and Veterinary Medicine, Romania)
- P06. Hepatitis E Virus Presence in Galician (NW Spain) Shellfish
Rivadulla E (Universidade de Santiago de Compostela, Spain)
- P07. Acute hepatitis E in French patients: epidemiology and neurological manifestations
*Abravanel F (Centre Hospitalier Universitaire de Toulouse, France) *Best Poster Award*
- P08. Changeable etiology of acute viral hepatitis: current role of Hepatitis E Virus
Fradejas I (Hospital Universitario 12 de Octubre, Spain)
- P09. Hepatitis E virus in sympatric cattle and wild ungulates in the Doñana National Park, Spain
Caballero J (Universidad de Córdoba, Spain)
- P10. Detection and quantification of hepatitis E virus and other foodborne viruses in food and clinical matrices – utilization of home-made MS2 phage-like particles
Mikel P (Veterinary Research Institute, Czech Republic)
- P11. Molecular epidemiology of hepatitis E virus in the Czech Republic
Vasickova P (Veterinary Research Institute, Czech Republic)
- P12. Antibodies against hepatitis E virus in Finnish moose
Oristo S (University of Helsinki, Finland)



- P13. Characterization of HEV in clinical samples and identification of food and environmental sources of HEV infections by applying metagenomics
Bofill-Mas S (University of Barcelona, Spain)
- P14. Improvement of Hepatitis E virus genotyping and subtyping
Piriz-Ruzo S (Vall d'Hebron Research Institute - Hospital Universitari Vall d'Hebron, Spain)



P01

Swine and wild boars as potential zoonotic reservoir of hepatitis E in Romania

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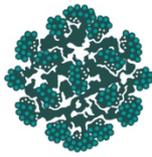
²Animal Health Laboratory. UMR 1161 Virology. ANSES, Maisons-Alfort, France

Hepatitis E virus (HEV) is an important public health concern in many industrialized countries. Domestic pigs are the main animal reservoirs of hepatitis E virus (HEV) in the European Countries. Wild boars are also an important reservoir, but their meat is less commonly consumed. Food-borne transmission appears to be the major pathway for human HEV infections in Europe. Raw or undercooked pork meat or pork liver are the most frequently reported food products associated with HEV sporadic cases.

Serological and molecular investigations of hepatitis E virus were carried out for the purpose of highlighting the role of domestic pig and wild boar as HEV reservoir in Romania. Our serological studies consisted in serological testing for the detection of HEV IgG antibodies in farm and backyard pigs, and wild boars from Eastern Romanian Counties. Swine HEV seroprevalence rates varied between 22,66% and 50%, depending of the breeding system, county and studied period. In wild boars the overall seroprevalence of HEV IgG-antibodies was 12,26% (26 out of 212), with minor difference rates between the five sampled Counties.

Molecular detection of swine HEV consisted in detection of an HEV ORF2 sequence by nested reverse transcription PCR using degenerate primers described by Cooper K. et al, 2005. The results revealed HEV presence both in farm pigs and wild boars, all sequenced strains belonging to genotype 3, respectively clustering in two groups 3a and 3chi.

Globally, our studies highlight that swine and wild boar HEV represents an important reservoir for genotypes 3, suggesting that these animal species pose a zoonotic risk and raise public health concern



P02

Risks, burden and socio-biology of hepatitis E infection in England

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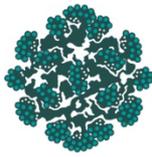
² Blood Safety, Hepatitis, Sexually Transmitted Infections (STI) and HIV Service
National Infection Service, Public Health England

³ Microbiology Services, NHS Blood and Transplant

Since 2010, a substantial increase in autochthonous cases of hepatitis E virus (HEV) has been observed across Europe and has brought to light a previously unrecognised public health threat. In England, an increase in acute HEV cases has been associated with the emergence of a novel clade G3.2. Acute HEV infections in England have been shown to be associated with the consumption of processed pork products. The potential for transmission of HEV and the clinical consequences of HEV positive blood components has been recognised and screening of blood donations for HEV began in 2016. The likely burden of HEV in England has been estimated to be between 100,000 and 150,000 infections annually. While a high proportion of HEV infections are asymptomatic, severe or chronic infections have been observed in immunocompromised individuals, highlighting the need for a greater understanding of the epidemiology of this disease.

Donor-cases identified through the screening programme were sent a link to a web-survey questionnaire. Information on a history of recent travel, food consumption, animal contact, environmental exposures, alcohol intake, medication and co-morbidities was gathered.

The epidemiology of autochthonous HEV infections in blood donors in England over an 18 month period was analysed. Donor cases were largely asymptomatic, and in those with symptoms infection was self-limiting. The majority of individuals reported consuming pork products in the nine weeks preceding blood donation. Further analysis is ongoing, and a case-control study is ongoing to further define the risk factors for acquisition of HEV infection.



P03

Use of liver transudation as an alternative matrix for the diagnosis of Hepatitis E using a commercial ELISA kit

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⁴ Instituto Tecnológico Agrario de Castilla y León ITACyL, Laboratory of Molecular Biology and Microbiology, Valladolid, Spain

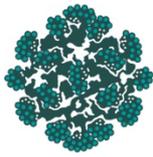
Hepatitis E is a viral disease currently considered an emerging zoonosis in industrialized countries. It is worldwide distributed and responsible of epidemics in developing countries and of sporadic outbreaks in developed countries. The transmission routes differ according to the area of appearance. Thus, in developing countries the transmission results from the consumption of contaminated water, while in developed countries is linked to the consumption of raw or undercooked food, specially pig liver and derived products, but also wild boar and deer ones. The most commonly used diagnostic technique is the ELISA test in serum samples, although ELISAs in meat juice samples have also been described. However, in certain cases the optimal collection of serum is not possible.

The aim of the present study is to validate the use of the liver transudate as an alternative matrix to serum for diagnosis of Hepatitis E in animals, as well to determinate the optimal dilution to be used.

For its implementation, sera and liver transudate samples were collected from 94 animals: 25 iberian pigs, 25 wild boars and 44 white pigs. A commercial ELISA kit (iDvet) was used for the analysis of both type of samples. Results obtained from the serum analysis were compared with those of undiluted transudate as well as at different dilutions (1:2, 1:10, 1:20). The agreement between the qualitative results (sera vs. liver transudate at different dilutions) was measured using the Kappa statistic and, for the comparison of the corresponding optical densities, the Intraclass Correlation Coefficient (ICC) was employed.

The highest agreement, according to the ELISA results in sera samples, was observed with liver transudate at a dilution of 1:10, in terms of both seropositivity and optical densities, with kappa coefficients and ICC higher than 0.728 and 0.864, respectively, even though slightly differences were observed between iberian pig and wild boar with the white pigs.

Our results demonstrate that liver transudate at a 1:10 dilution may be an interesting alternative for the detection of anti-Hepatitis E virus antibodies by ELISA in swine and wild boars, although further studies should be carried out in this regard.



P05

Human hepatitis E in Romania: autochthonous or/and imported?

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Hepatitis E virus infection is one of the leading causes of acute viral hepatitis worldwide. In Europe, autochthonous HEV infection is considered an emerging disease, HEV-3 being the most prevalent genotype. Over the past 10 years, more than 21,000 cases of acute hepatitis E have been reported in EU/EEA. The increasing number of hepatitis E cases has been associated with presence of HEV in animals. Of the 30 countries from which these data were collected, 20 have specific surveillance systems and well-established diagnosis protocols.

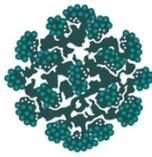
In Romania, the absence of an evaluation and reporting program for hepatitis E makes this disease underdiagnosed. Moreover, the importance of each high-risk source of virus for public health in Romania is not fully known. Nevertheless, the HEV infection has been investigated in humans and swine (pig and wild boar), most of researches being carried out in populations from Eastern Counties.

The serological studies conducted in human population revealed various aspects. Thus, the first investigation on HEV infection in Eastern Romania revealed the presence of HEV IgG antibodies in 5.9% of general population tested (4/67) and the second one highlighted a 12% prevalence (3/25) in patients diagnosed previously with hepatitis B or C.

Studies carried on human hepatitis E infection in north-eastern Romania highlighted that HEV IgG antibodies prevalence in general population was estimated in 2011 at 17,14% (12/70), whereas in 2012 the recorded prevalence was 12,82% (10/78). These investigations were carried out along with those in the domestic swine and led to the suspicion of a possible association of the human's infection with the presence swine HEV. This hypothesis was sustained later by genetically relatedness between wild boar and swine romanian HEV strains to human HEV strains circulating in Europe.

Currently, serological and molecular investigations conducted in different patient groups from Eastern Romania revealed an increased rate of HEV infection. Total HEV antibodies prevalence in patients with acute hepatitis of unknown ethology was 29.16%, respectively 32.5% in general population. The two human HEV isolates genetically characterized clustered into subtype HEV-3c, the most prevalent subtype identified in Europe.

All data on human HEV in Romania correlated with the reports of European Food Safety Authority (EFSA) and our previous results on animal HEV may lead to two hypothesis suggesting that the infection may be associated with pork and pork meat imports from EU countries, but also supports the native infection hypothesis.



P06

Hepatitis E Virus Presence in Galician (NW Spain) Shellfish

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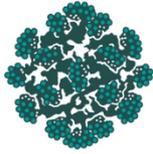
Hepatitis E virus (HEV) was first documented from a patient with enterically transmitted non-A, non-B hepatitis in 1989 and nowadays, is the most common cause of viral enterically transmitted hepatitis around the world. According with the World Health Organization, HEV affects almost 20 million individuals annually, causing acute liver injuries in approximately 3.3 million and 56.600 deaths, with the subsequent healthcare associated economic losses. Genotypes 1 and 2 are prevalent in developing countries, where hepatitis E is highly endemic. Until recently, in industrialized countries HEV had been exclusively considered in travelers returning from endemic regions, but the discovery of zoonotic transmission of autochthonous genotype 3 HEV has changed the comprehension of HEV infection in these regions. In fact, HEV genotype 3 are widely present in swine to such an extent that they are now considered important reservoirs for human disease.

Coastal waters are often contaminated not only with effluents from sewage treatment plants, but also by runoffs following manure application. When grown in these polluted waters, bivalve molluscs can bioaccumulate human pathogens like enteric viruses due their filter-feeding nature. The facts that virus persist in these organisms for long periods and that depuration does not completely eliminate viral particles cause that molluscs become an important vector for enteric diseases, especially when consumed raw or lightly cooked.

A total of 168 samples obtained from two different Galician rías, one in the North (Ría de Ares-Betanzos) and the other in the South (Ría de Vigo), were analysed by Real-time reverse transcription-quantitative PCR. These samples included wild- and raft-cultured Mediterranean mussels, Manila and carpet-shell clams and cockles, collected from different harvesting areas. All sampling points were classified as B (230–4600 CFU *Escherichia coli* per 100 g shellfish) according to the European legislation and shellfish were collected monthly for 18 months, from January 2011 to June 2012.

HEV was detected in 41 out of 168 (24.4%) samples. Cultured mussels were contaminated in 20 of 70 (28,6%) samples, wild mussels in 13 out of 35 (37,14%) samples, clams in 5 out of 31 (16,12%) samples, and cockles in 3 out of 32 (9,37%) samples. HEV prevalence was slightly higher in the South estuary. Quantification levels ranged from $5,80 \times 10^3$ to $1,08 \times 10^6$ RNAc/g tissue, the highest values being observed for the clam samples.

Although depuration is mandatory for class B harvested molluscs, such process has proved to be ineffective for a total viral elimination. Further studies are needed for a better understanding of the significance of the HEV presence in shellfish as well as to determine the potential risks for human health.



P07

Acute hepatitis E in French patients: epidemiology and neurological manifestations

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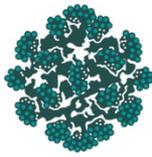
Hepatitis E virus (HEV) is a major cause of acute hepatitis worldwide. However, our understanding of the source of contamination is incomplete and the frequency of neurological manifestations is still unknown.

200 eligible cases were reported to the French national Reference Center from January 2015 to December 2015 were prospectively included in this case-control study (1 case: 1 control, matched for sex, age and area of living) to investigate the risk of infection. We documented the factors associated with their HEV infection and clinical manifestations.

The 200 HEV-infected patients included 137 who were immunocompetent and 63 immunocompromised. The factors associated with an HEV infection were contact with farm animals, eating pork liver sausage and eating unpeeled fruit. The 33 patients (16.5%) who reported neurological symptoms included 14 with neuropathic pain suggesting small fiber neuropathy, 9 with painless sensory disorders, 6 with Parsonage-Turner syndrome, one Guillain-Barre syndrome, one meningitis, one encephalitis and one diplopia. Neurological manifestations were more frequent in immunocompetent patients (22.6% vs 3.2%, $p < 0.001$).

This study highlights the risk of HEV transmission by the environment in industrialized countries. The higher frequency of neurological disorders in immunocompetent patients suggests pathophysiological mechanisms involving the immune system.





P08

Changeable etiology of acute viral hepatitis: current role of Hepatitis E Virus

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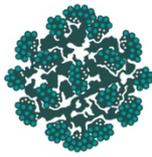
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The importance of the hepatitis E virus (HEV) as a cause of acute hepatitis is barely known in our country, since it is not usually included in routine immunodiagnosis. Before incorporating the HEV diagnostic tests in the routine serological profile for viral hepatitis, a pilot study was carried out to evaluate the relative importance of the different hepatotropic viruses (A, B, C, D and E) in the etiology of acute hepatitis.

A retrospective study from January 2013 to December 2014 was conducted in Hospital Universitario 12 de Octubre (Madrid, Spain). All patients attending Emergency Services and Primary Care Centers attached to our hospital with serum levels of alanine aminotransferase (ALT) 10x higher than the normal limit and with a requested serological profile for viral hepatitis were included. Medical records (including serological history and follow-up) of patients were reviewed.

In the period of study, 273 patients were included. 46 cases of acute viral hepatitis were detected: 14 (30.4%) hepatitis A, 10 (21.7%) hepatitis B, 7 (15.2%) hepatitis C, 0 hepatitis D and 15 (32.6%) hepatitis E. All the cases of acute hepatitis E were patients older than 40 years, 11 (73.3%) were men, 14 (93.3%) were autochthonous cases, 8 (53.3%) had liver disease (cirrhosis or hepatic steatosis) prior hepatitis E infection and 1 was a hepatic transplant recipient.

HEV is a frequent cause of episodes of acute hepatitis in our setting. We believe that serological tests for HEV should be included in the routine study of acute adult hepatitis.



P09

Hepatitis E virus in sympatric cattle and wild ungulates in the Doñana National Park, Spain

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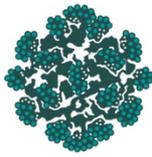
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Hepatitis E (HE) is an emerging and mainly foodborne disease in industrialized countries of Public Health concern. Although domestic pigs and wild boar are considered the main reservoir of zoonotic HE virus (HEV) genotypes, information about the role of other animal species is still very scarce. Here, we aimed to assess HEV circulation in sympatric domestic and wild ungulates in the Doñana National Park (DNP), Spain. Blood samples from 439 ungulates, including 137 cattle (*Bos taurus*), 101 red deer (*Cervus elaphus*), 102 fallow deer (*Dama dama*) and 99 wild boars (*Sus scrofa*) were collected in the DNP during 2015. Sera were analyzed in parallel using an indirect ELISA and real time RT-PCR.

A total of 59 of the 439 (13.4%; CI_{95%}: 10.3-16.6%) tested animals had antibodies against HEV. By species, the seroprevalence was 12.4 ± 5.5% in cattle (17/137), 29.7 ± 8.9% in red deer (30/101), 1 ± 1.9% in fallow deer (1/102) and 11.1 ± 6.2% in wild boar (11/99). Significantly higher seropositivity was found in red deer compared with the other species (P<0.001). HEV RNA was detected in 20 animals (4.6%; CI_{95%}: 2.6-6.5%). HEV active infection was found in 9.5 ± 4.9% of cattle (13/137), 5.0 ± 4.2% of red deer (5/101), 1.0 ± 1.9% of fallow deer (1/102) and 1.0 ± 2.0% of wild boar (1/99). The phylogenetic analysis performed in the RNA-positive wild boar showed that the sequence isolated belonged to zoonotic genotype 3, clade 3abchij.

The results pointed out widespread HEV circulation in the DNP. HEV exposure and active infection were evidenced in the four sampled ungulate species, confirming for the first time HEV infection in cattle in Europe. Further studies are required to elucidate the role of this species in the epidemiology of HEV and to assess the zoonotic risk of HEV transmission through the consumption of cattle products in Spain.



P10

Detection and quantification of hepatitis E virus and other foodborne viruses in food and clinical matrices – utilization of home-made MS2 phage-like particles

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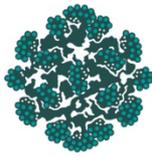
The detection and quantification of foodborne viruses in food and clinical matrices represents relatively complex, multi-step analysis which is most often ended by detection and quantification of these viruses by the real-time quantitative reverse transcription polymerase chain reaction (RT-qPCR).

To identify false negative results and to guarantee the validity and reliability of obtained results it is necessary to strictly control the entire analytical process. Therefore, an external control spanning/including all analytical procedures should be used for this purpose. According to ISO technical specification (ISO/TS), in the case of RT-qPCR detection of hepatitis A virus (HAV) and noroviruses (NoV), such a control is characterised as non-pathogenic virus or virus-like particle with structural properties close to those of pathogenic virus (non-enveloped, +ssRNA genome), which should not be expected to occur naturally in matrices under test while being genetically distinct from the pathogenic virus in order to be able to be reliably differentiated from it by molecular biological methods. The ISO/TS recommend using a mutant strain of mengovirus (vMC0) for this purpose.

The external control of analysis fulfilling these criteria was prepared in the form of MS2 phage-like particles (MS2 PLP), which were derived from bacteriophage MS2. The MS2 PLP were compared to vMC0. The prepared MS2 PLP carry the unique control *de novo*-synthesized +ssRNA sequence within the capsid whose natural occurrence in the analysed sample is extremely unlikely and can therefore be used as the universal external control of analysis in RT-qPCR detection and quantification of non-enveloped +ssRNA foodborne viruses including hepatitis E virus (HEV). Since there is no ISO/TS for detection of HEV so far, the use of external control of analysis in detection of HEV is essential as well as in the detection of HAV and NoV according to existing ISO/TS.

MS2 PLP can be used to accurately determine the efficiency of the whole analytical process for different types of matrices. Moreover, the accurate value of the efficiency of the process enabled to determine the HEV viral load in each analysed sample. In addition to this use, improved system for production of MS2 PLP can be simply modified to produce MS2 PLP carrying other specific +ssRNA molecules e.g. target sequences of established RT-qPCR detection methods. MS2 PLP are extremely pure without the presence of contaminating DNA molecules and are produced in total quantity up to 10^{14} of MS2 PLP in the single production batch. Therefore, MS2 PLP can be utilized also as a standard and/or positive control in established RT-qPCR detection methods or as a calibrator in optimizing detection methods of foodborne +ssRNA viruses in different matrices.

This work was supported by the grant No. 17-31921A provided by Ministry of Health of the Czech Republic.



P11

Molecular epidemiology of hepatitis E virus in the Czech Republic

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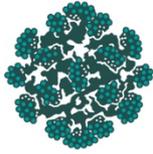
Hepatitis E virus (HEV) is causative agent of an important public health problem worldwide. Although this infection has at least two epidemiological profiles, food-borne transmission of HEV appears to be the major route in European countries. Molecular epidemiology comparing virus sequences derived from human patients and different animal species provides evidence of zoonotic potential and main sources of the virus in Europe; domestic pigs and wild boars.

Based on this knowledge, extensive genomic variability among HEV and their known geographical distribution, the objectives of our studies were to perform sequence and phylogenetic analyses of HEV originating from clinical samples of Czech patients with acute hepatitis E, to compare obtained sequences with HEV sequences originating from Czech domestic pigs and wild animals and thus attempt to determine the origin of the infection.

Between years 2012 and 2017 a total of 160 partial sequences of HEV ORF1 originating from human patients were analysed. The sequence and phylogenetic analyses showed that 152 HEV sequences belonged to HEV-3. Obtained sequences were phylogenetically related to HEV found in Czech domestic pigs and wild boars or to HEV strains from other European countries. Simultaneously specific geographic distribution of particular HEV strains was observed within the Czech Republic; specific clusters from North Moravia and Central Bohemia. These clusters included HEV found in biological samples of human and animal origin, which supports the hypothesis of interspecies transmission of HEV also in the Czech Republic.

During this period of six years, only eight imported HEV infections were identified. HEV-1 was found in clinical samples of seven patients and HEV-4 was detected once. A relationship with the Chinese and Indian HEV strains was revealed. These findings were confirmed by patients' anamnestic data; history of travel to China and India. According to information from the Czech central databases EPIDAT there is significantly increased number of autochthonous in the comparison with imported hepatitis E cases in the Czech Republic; approximately 88 % of reported cases are of autochthonous origin. Therefore, obtained results are in agreement with the national database report.

This work was supported by grant AZV CR 17-31921A.



P12

Antibodies against hepatitis E virus in Finnish moose

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Some hepatitis E viruses (HEV) are zoonotic. With the exception of pigs and wild boars, the animal reservoirs for these viruses are not well known. Several studies have reported the presence of HEV in cervids. Recently, hepatitis E virus of a potential new genotype was found in moose in Sweden. In this study, we analysed sera from Finnish moose and deer for anti-HEV-antibodies.

Our sampling frame was a cervid serum bank at the Faculty of Veterinary Medicine, University of Helsinki. We focused on three different regions in Finland, and randomly selected 162 moose (*Alces alces*) and 50 white-tailed deer (*Odocoileus virginianus*) into this study. We analysed the samples for total anti-HEV-antibodies using a double-sandwich ELISA assay.

Anti-HEV-antibodies were detected in 10 out of the 162 moose sera (6.2%), but not in any of the white-tailed deer sera. HEV-antibody-positive animals were detected in all three regions, indicating exposure could be widespread.

We could demonstrate the existence of anti-HEV-antibodies in Finnish moose sera, which suggests that HEV is circulating among moose. This is in agreement with the studies that demonstrated anti-HEV antibodies in moose in Sweden.



P13

Characterization of HEV in clinical samples and identification of food and environmental sources of HEV infections by applying metagenomics

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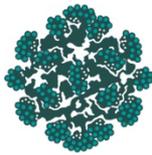
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We have developed mass sequencing protocols using paired end 300-base runs on the Illumina MiSeq platform with improved sample pre-treatments and bioinformatics pipelines for the identification of the viruses excreted in urban sewage that could contaminate irrigation water and fresh vegetables. By applying these tools, we have evaluated the applicability of metagenomics for the characterization of HEV as a water and/or food contaminant and as an etiological agent in acute hepatitis infections.

The sewage virome contained 41 viral families, including pathogenic viral species from families *Caliciviridae*, *Adenoviridae*, *Astroviridae*, *Picornaviridae*, *Polyomaviridae* and *Papillomaviridae*; virus of the *Hepeviridae* family, HEV-3, was identified in 2 of 5 sewage samples analyzed in the area of Barcelona. Conventional secondary wastewater treatment reduces viral concentration in outlet effluents but does not eliminate viruses, still representing a source of contamination. Interestingly, parsley plants irrigated with urban river water analysed by viral metagenomic means presented HEV sequences: several sequences related to hepatitis E genotype 3 ranging from 154 to 548 base pairs long were detected in parsley leaves. Those sequences matched up with variable identities at nucleotide levels ranging from 86 to 98% and clustered with HEV-3f. In addition, in a study analyzing irrigation water in Europe (METAWATER), the contamination of groundwater samples in an area with porcine farms was studied detecting a mean value of 10E+03 GC/L of porcine adenoviruses in 4/12 samples analyzed, probably related to the proximity of swine manure used as fertilizer, and HEV was detected in 1/12 of the samples analyzed.

The metagenomics protocol developed was also used to study pools of serum samples from 10 acute hepatitis patients infected with HEV in the same area. A total of 27 contigs were matched to sequences of the *Hepeviridae* family, 76.1% (5,508 of 7,238 bp) of the HEV whole genome was sequenced with an average pairwise identity of 85.5% against the genotype HEV-3f and other closely related genotypes. In addition, 3 contigs from an immunosuppressed patient's serums pool were also aligned with genotype 3a.

Viral metagenomics is a promising tool applicable to environmental surveillance, food-safety, outbreak investigation and clinical diagnostics of hepatitis patients. Further steps towards increasing the sensitivity of the technique, testing other sequencing platforms and evaluating the performance of existing software applications for data interpretation are our next goals.



P14

Improvement of Hepatitis E virus genotyping and subtyping

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Hepatitis E virus (HEV) is a major cause of morbidity and mortality and representing a global health problem, being along with hepatitis A the most common cause of acute hepatitis in Europe. Likewise, the HEV has a high seroprevalence in the population, probably due to the zoonotic character of two of the genotypes (genotype 3 and 4), and especially G3 which is the most frequent in the Spanish population. G3 uses several reservoir animals (pigs, rabbits, wild boar, etc.), being the pig the main reservoir and source of infection due to the consumption of its undercooked meat in the European population. This could be a possible explanation for the high prevalence highlighting the importance of the correct genotyping and subtyping of the virus.

Until now to carry out the genotyping and subtyping, primers designed for ORF2 were used but, due to the low variability of this part of the genome of the virus, many sequences remained without genotyping and/or subtyping.

Therefore, the objective of our study has been to design a useful diagnostic tool for the subtyping and correct classification of HEV genotype 3, the most common in Europe.

Thus, a set of HEV sequences previously published by Smith et al. were selected and a sliding windows analysis was carried out to verify which part of the virus genome is more discriminating between subtypes using the substitution method of Kimura and multidimensional scaling (MDS). The results of this analysis gave rise to a region of 400 nucleotides between bases 1890 and 2290 of ORF1, as the most discriminant one.

Once the region was selected, subtype-specific primers were designed to correctly differentiate and classify the subtypes (a-j) of genotype 3 of the HEV. The effectiveness of these primers is currently being tested through the amplification of samples from the Banc de Sang i Teixits of the Hospital Vall d'Hebron in order to validate the technique and implement this method of subtyping as a technique for the diagnosis of the HEV and classification method of the virus.



HEV2018

HEPATITIS E WORKSHOP
MADRID 4-5 JUNE 2018

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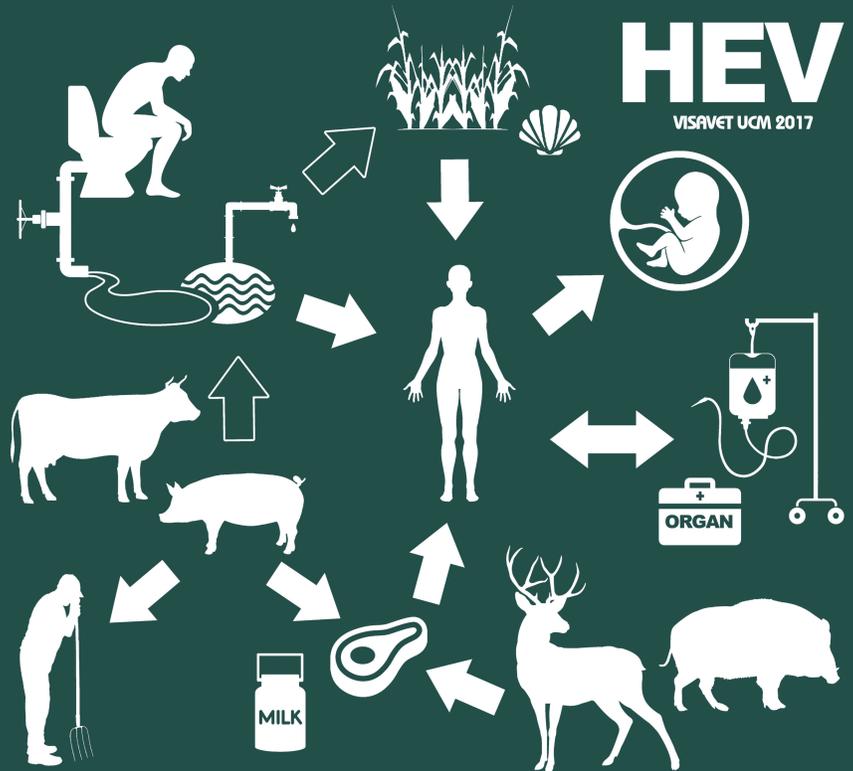


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The VISAVET centre of Complutense University of Madrid organize a MedVetNet workshop focused on HEV by a One Health approach (see programme), connecting professionals from different expertise areas (clinicians, veterinarians, epidemiologists, food officers and policy makers) from different European countries.

The global workshop objective will be to share and update the knowledge about HEV at European level with the ultimate goal of establishing a hepatitis E consortium and a network in order to apply for European calls (Horizon 2020).

Hepatitis E virus (HEV) is an under-recognised cause of acute hepatitis in high-income countries. Originally considered to be restricted to humans, it is now clear that HEV and HEV-like viruses have several animal reservoirs with complex ecology and genetic diversity. Although there is a single serotype, four major HEV genotypes (1-4) capable of infecting humans are currently recognized. Genotype 3 predominates in high-income countries, including those in Europe. Transmission of this genotype is usually zoonotic and has been linked mainly to the consumption of pork products, but also to wild boar, deer or shellfish. EFSA has recently published a scientific report, which highlights a Europe-wide increase in cases and emphasizes the need for more research efforts on the epidemiology, diagnosis and control of HEV. Standardised case definitions and testing policies (including the development, harmonization and standardization of the detection methodology) would allow a better understanding of the epidemiology of HEV as an emerging cause of liver-related morbidity in Europe. Despite of major recent developments in the epidemiology, treatment, and prevention of hepatitis E, some other gaps in knowledge need to be addressed (effective HEV control in meat production chains, need of blood products screening, refinement of treatment paradigms of acute and chronic hepatitis E, etc.)



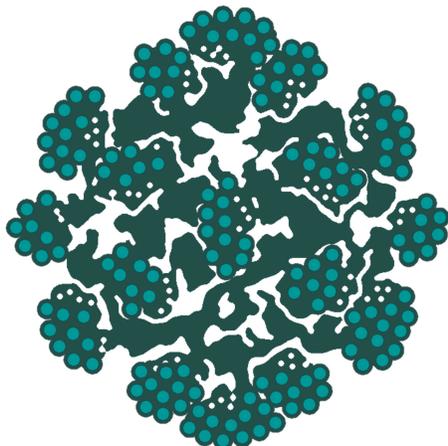
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