# IAFP's European Symposium on Food Safety

# S6 – Determining the Efficacy of Control Measures against foodborne viruses

## The trouble with Hepatitis E virus!

05/04/22

Prof Linda Scobie

GCU Glasgow Caledonian University

University for the Common Good

Munich GERMANY 4-6 May 2022 IAFP'S EUROPEAN SYMPOSIUM ON FOOD SAFETY

# History of Hepatitis E virus

- First recognised as responsible for an outbreak in New Delhi in 1955
- Recognised as non A non B hepatitis in 1980s….

*Original Paper*

**Evidence for a Virus in Non-A, Non-B Hepatitis Transmitted via the Fecal-Oral Route**

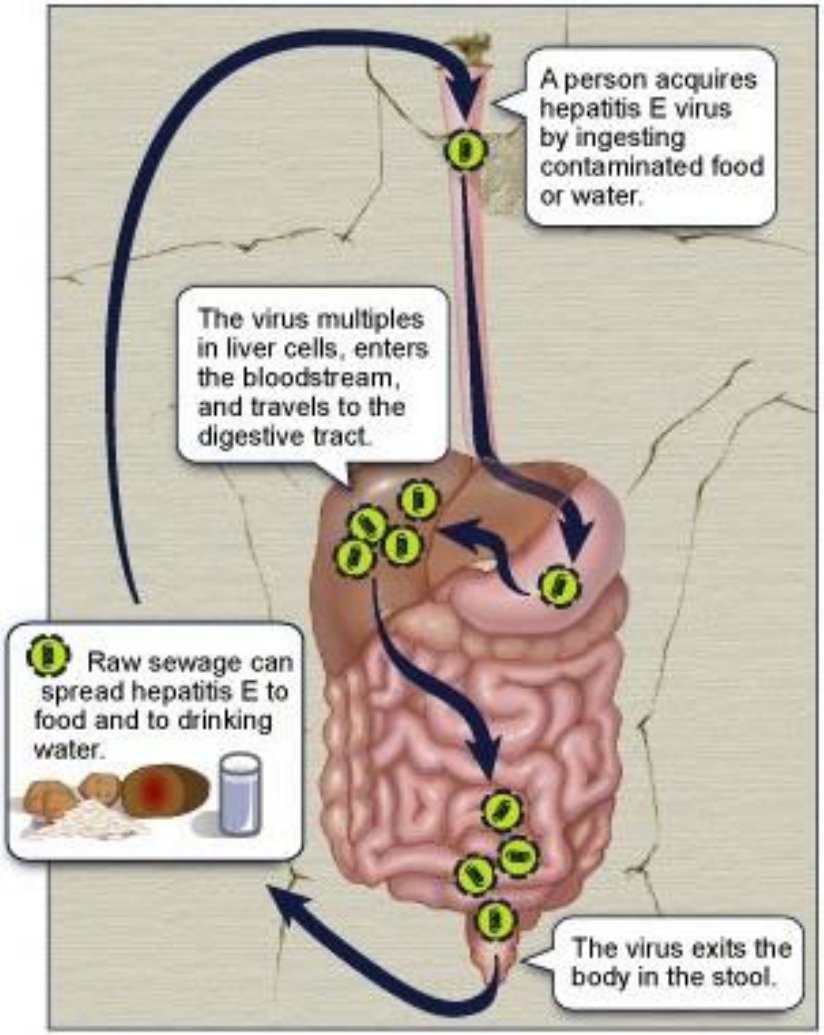
M.S. Balayan[a], A.G. Andjaparidze[a], S.S. Savinskaya[a], E.S Ketiladze[b], D.M. Braginsky[b], A.P. Savinov[a], V.F. Poleschuk[a]

[a]Institute of Poliomyelitis and Viral Encephalitides, and
[b]D.I. Ivanovsky Institute of Virology, USSR Academy of Medical Sciences, Moscow, USSR

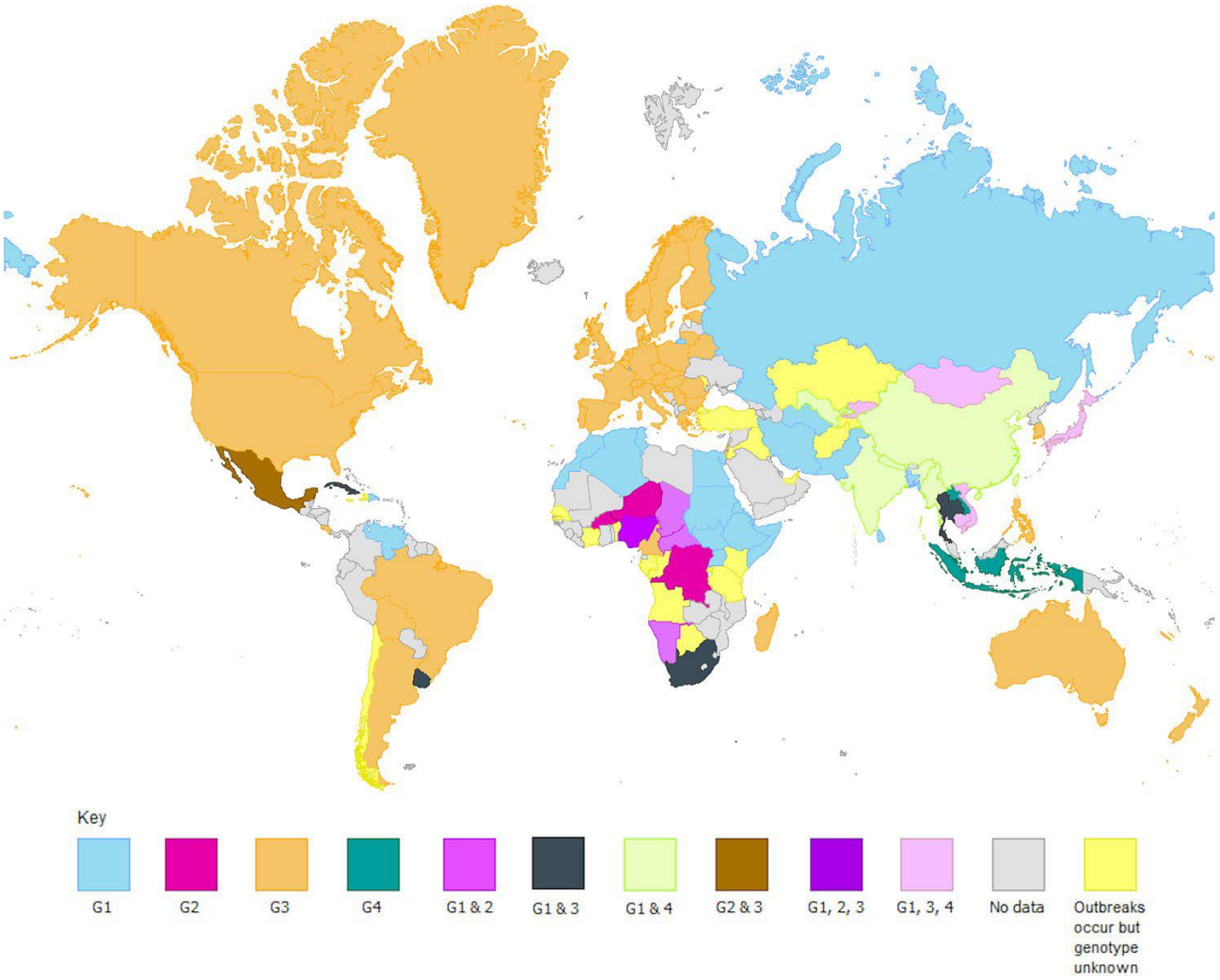
Address of Corresponding Author

*Intervirology* 1983;20:23-31 (DOI: 10.1159/000149370)

- In 1990s classified as new hepatic virus - Hepevirus



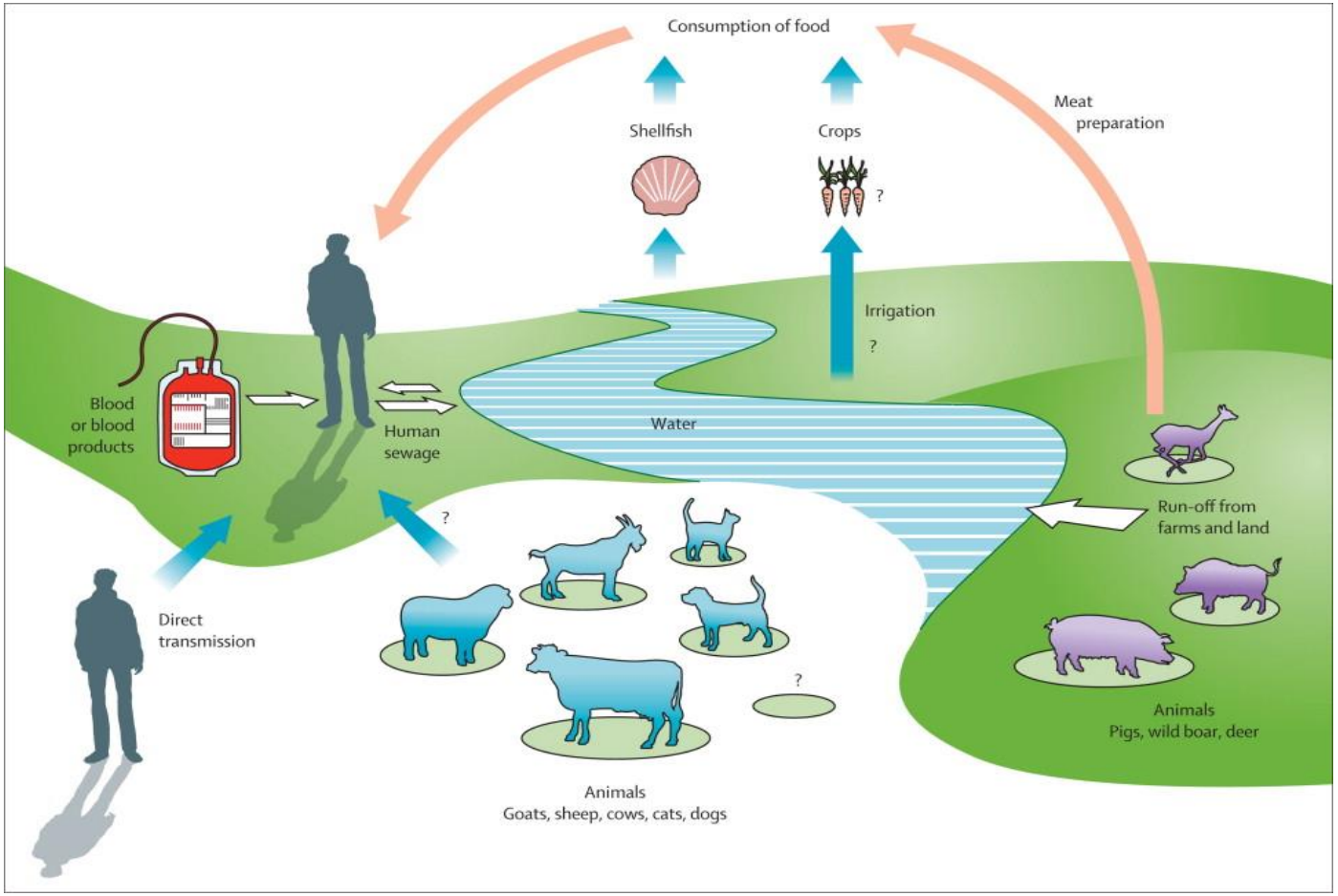
# Genotypes





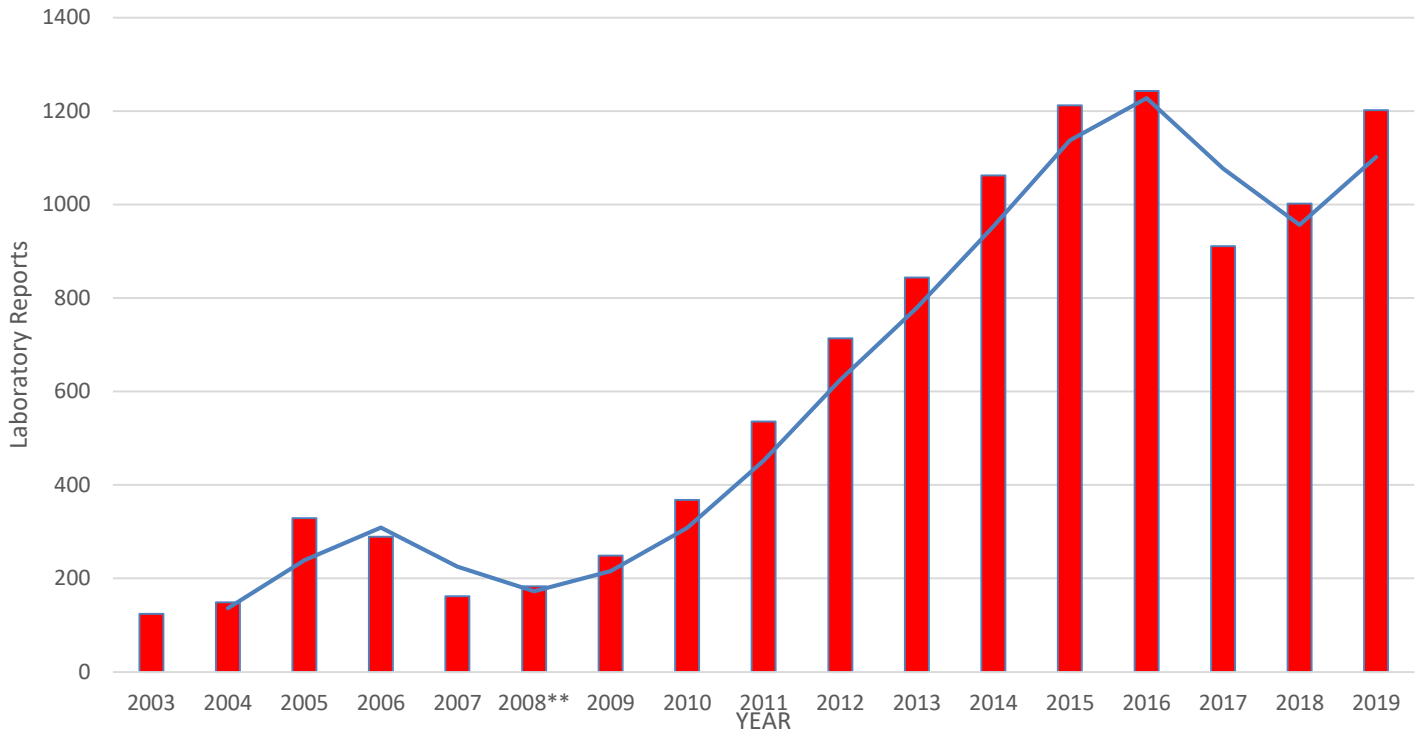

From Treagus et al; 2021, Food and Environmental Virology (2021) 13:127–145

# Why is it important?
# Transmission Routes



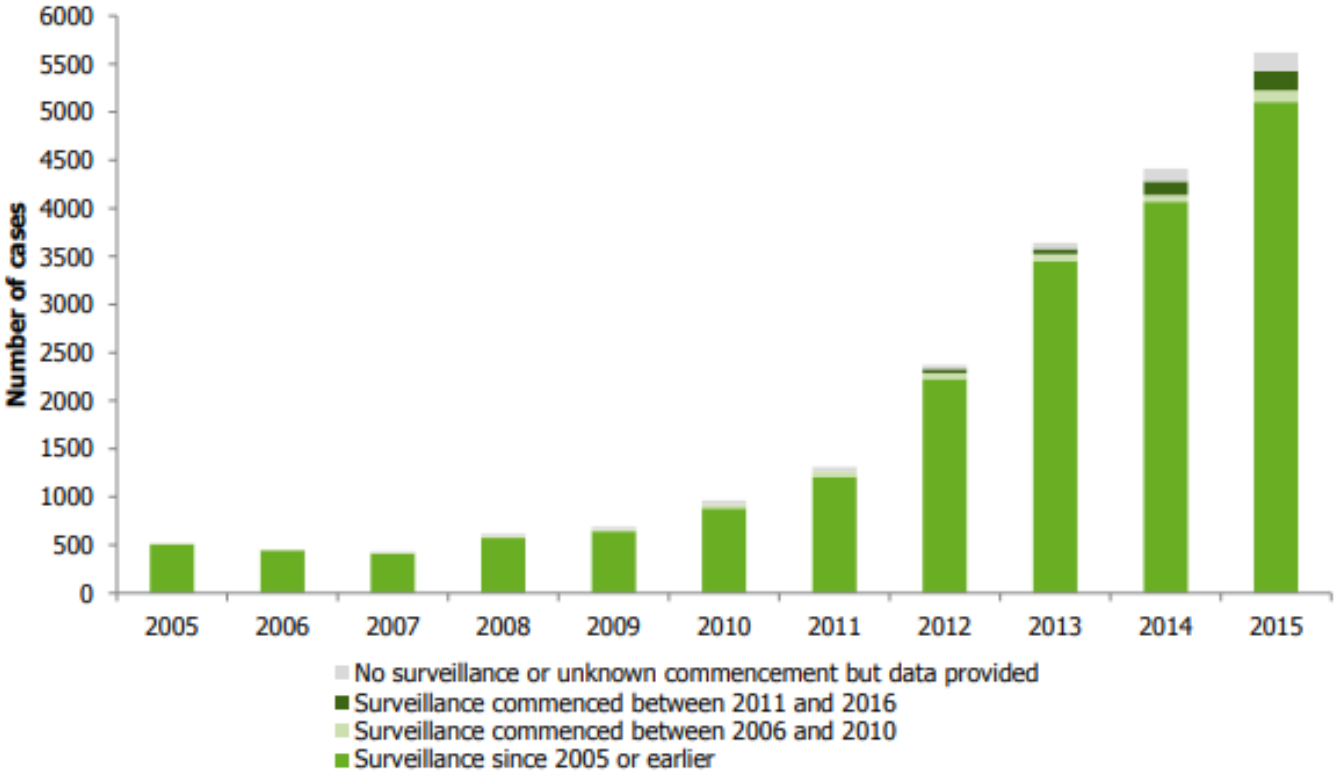
Glasgow Caledonian University
University for the Common Good

# Why is it important?
# Laboratory reported incidence




**Every year there are an estimated 20 million HEV infections worldwide, leading to an estimated 3.3 million symptomatic cases of hepatitis E.**
**WHO estimates that hepatitis E caused approximately 44 000 deaths in 2015 (accounting for 3.3% of the mortality due to viral hepatitis).**

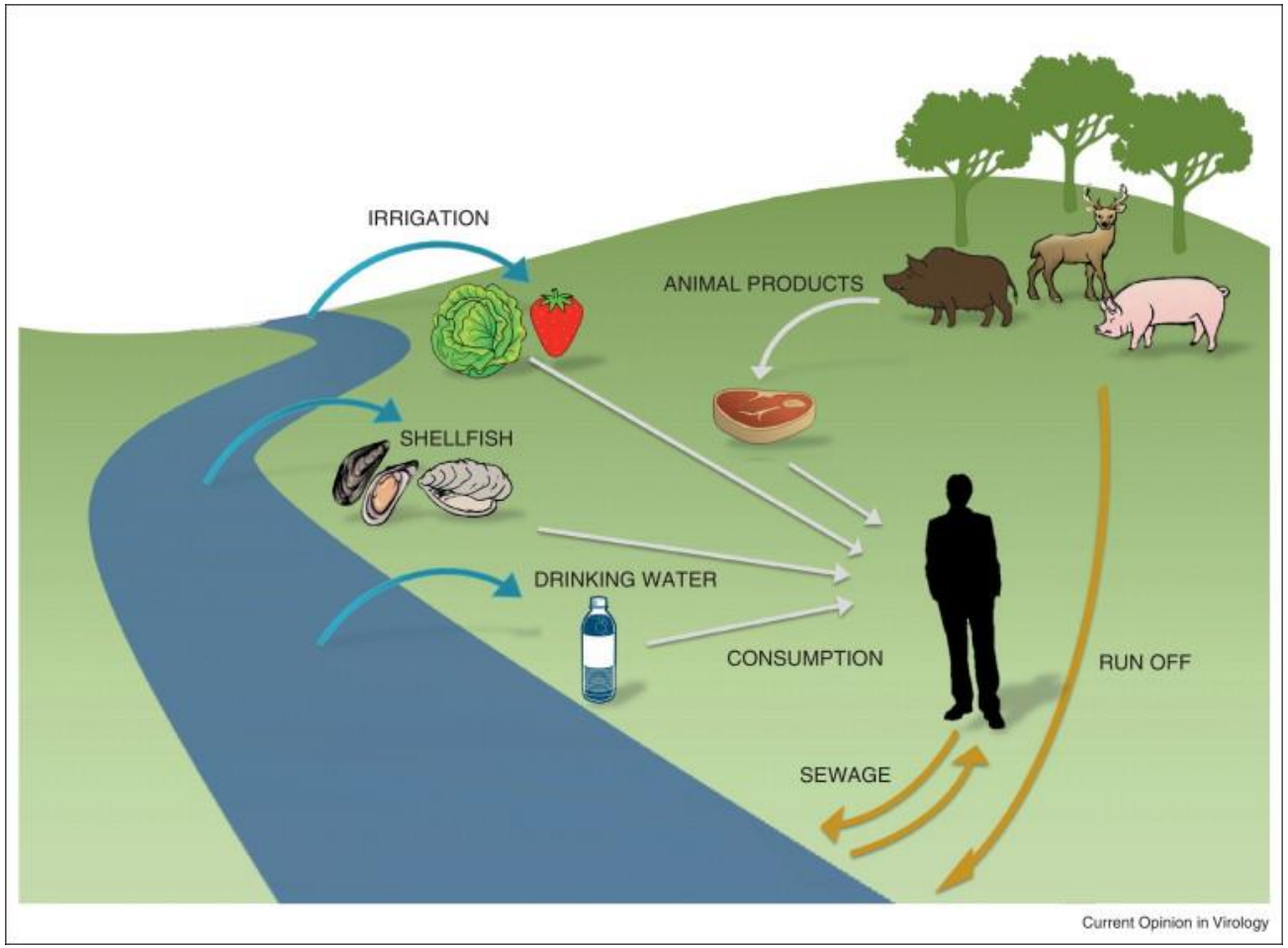
**Figure 3.2. Annual number of confirmed cases of hepatitis E by year of commencement of surveillance, EU/EEA Member States, 2005–2015 ***




** Data available for: Austria, Belgium, Bulgaria, Croatia, Cyprus, Czech Republic, Estonia, Finland, France, Germany, Hungary, Italy, Latvia, the Netherlands, Norway, Poland, Portugal, Slovakia, Slovenia, Spain, Sweden, and the United Kingdom.*

https://www.ecdc.europa.eu/sites/default/files/documents/HEV_Surveillance-report-2005-2015.pdf

# Why is it important?
# Links to the food chain



# One in ten sausages may carry the hepatitis virus: Cases of rare deadly strain have rocketed 40% in a year

- Once considered very rare, cases have risen by nearly 40 per cent in a year
- 1 in 50 of those infected will die, rising to one in five pregnant women
- Sausages most dangerous pork product - they contain liver meat

By SOPHIE BORLAND FOR THE DAILY MAIL

**PUBLISHED:** 17:52, 15 September 2013 | **UPDATED:** 22:35, 15 September 2013

Share

181 View comments

As many as one in ten sausages could be infected with a potentially deadly virus that causes liver damage, scientists warn.

They are concerned that rising numbers of Britons are being struck down with hepatitis E after eating contaminated pork.

The infection was once considered very rare but cases have risen by nearly 40 per cent in a year and there were 657 in 2012.

The virus usually causes only relatively mild symptoms such as sickness, a temperature and muscle pain, which clear up by themselves within a month.

But it can be fatal for the elderly, cancer victims, pregnant women and others with existing liver problems.

Around one in 50 of those infected will die, rising to one in five pregnant women.

Experts say sausages have to be cooked at 70C (158F) for at least 20 minutes to kill the virus but they say that most Britons do not leave them in the oven for this long.

Tests have showed that it can survive at 60C (140F) after an hour.

Deadly porker: One in ten sausages could be carriers of hepatitis E

A report published last week by the Department for Environment, Food, and Rural Affairs says 10 per cent of sausages sampled were found to contain the virus.

It states that there is 'increasing evidence' that hepatitis E is a food-borne infection.

Daily Scottish Mail
Section: News
Edition: 01
Date: 13 May 2015
Page: 37
Circulation: 165,610
Source: ABC Sep 2014
pressdata

# Tenfold rise in cases of hepatitis E

## Shellfish linked to increase

By Victoria Allen
Scottish Health Reporter

AN explosion of cases of hepatitis E in Scotland has been linked to shellfish caught off the coast.

More than ten times the number of people are being diagnosed with the virus, also believed to be present in one in ten sausages.

Cases of hepatitis E, which causes liver problems such as jaundice and can be fatal in pregnant women, have leapt from 13 in 2011 to 161 last year.

More than a third of those affected were men aged over 65.

The virus is thought to be found in 65 per cent of pigs, making sausages, pork and salami a potential source. It is also found in undercooked game meat, such as grouse from shooting estates, and processed shellfish.

A study from 2012 found a large number of mussels collected off the West Coast contained the hepatitis E virus. Shellfish can become contaminated if the water has been polluted with sewage or animal waste.

However, it is not definitively known what has caused the surge in infection among Scots, only part of which is attributed to better patient screening and reporting.

Dr Jacqui McElhinney, of Food Standards Scotland (FSS), said: "Hepatitis E can be transmitted in a number of different ways, including poor sanitation and the consumption of contaminated food. FSS and Health Protection Scotland (HPS) are working with other partners to develop research which will improve our understanding of the main risk factors for hepatitis E infection."

Experts say as many as 65,000 victims every year in Britain unknowingly contract the virus, which affects more men than women.

The 2012 study, published in the journal Emerging Infectious Diseases, examined mussels collected from five tidal locations in Scotland, including one close to a slaughterhouse and meat processing plant.

All but three of 39 mussels from the West Coast and five of the nine taken from the East Coast tested positive for hepatitis E, although it is not certain if the virus would have caused illness in humans.

Experts say conventional cooking methods are unlikely to kill off the virus, while the Sustainable Food Trust claims cramped factory farms help it to spread.

Healthcare Improvement Scotland said: "HPS has established a multi-agency group including representatives from the Scottish Government and FSS to identify ways to reduce the number of new cases.

"We recommend practising good hand hygiene and following FSS advice about the preparation and handling of food."

victoria@dailymail.co.uk



THE TIMES

The Times (London)
July 26, 2016 Tuesday
Edition 1;
National Edition

**Why your summer barbecue might give you hepatitis E**

GCU Glasgow Caledonian University

University for the Common Good

# Evidence of Foodborne Transmission

- First identified in Japan – undercooked Sika deer meat
- Wild boar - pig liver - Japan
- Pig liver sausage – France
- Pork meat - Spain

**Zoonotic transmission of hepatitis E virus from deer to human beings**

*Shuchin Tei, Naoto Kitajima, Kazuaki Takahashi, Shunji Mishiro*

**Zoonosis has been suggested for hepatitis E virus (HEV) infection, but so far is based only on indirect evidence. We experienced a series of cases of HEV infection among people who had eaten uncooked deer meat 6–7 weeks before. On testing, a left over portion of the deer meat, kept frozen to eat in the future, was positive for HEV RNA, whose nucleotide sequence was identical to those from the patients. Patients' family members who ate none or very little of the deer meat remained uninfected. These findings provide direct evidence for HEV infection to be a zoonosis.**

*Lancet* 2003; **362:** 371–73

Hepatitis E virus (HEV) infections, which are endemic and frequently epidemic in developing countries, are seen also in developed countries, but generally in the form of sporadic acute or fulminant hepatitis. Some cases in developed countries occur in people who have travelled to endemic areas, but others are of domestic infection, for which the method of transmission remains obscure.[1-3] Since HEV or like viruses and antibodies to HEV have been noted in a wide variety of animals, especially swine, a hypothesis has arisen that zoonosis is involved in the transmission of HEV, especially for the cases in non-endemic areas. This hypothesis is based on indirect evidence, such as the high frequency of antibodies to HEV in animal handlers and that the local pig strains are homologous to human strains in the same districts.[4] We report direct evidence of zoonotic transmission.

A man aged 44 years (patient O-1, table) visited one of our hospitals on April 16, 2003, complaining of fever, nausea, and general malaise. Diagnosis of acute hepatitis was easily established based on raised liver enzymes and bilirubin. While he was recovering, his father (O-2) came to us on April 25 with symptoms and signs similar to his son's. Moreover, within 1 week after that, one of the brothers of the index patient (O-3) and his friend (H-6) also presented with hepatitis. All patients were negative for serological markers of hepatitis A, B, and C viruses when tested on admission. Later, however, all the serum samples obtained from these patients on April 29 were positive for HEV RNA and for IgM and IgG antibodies to HEV, leading to the diagnosis of hepatitis E.


**Hepatitis E Virus Transmission from Wild Boar Meat**

**Tian-Cheng Li,* Katsumi Chijiwa,† Nobuyuki Sera,† Tetsuya Ishibashi,† Yoshiki Etoh,† Yuji Shinohara,‡ Yasuo Kurata,‡ Miki Ishida,§ Shigeru Sakamoto,¶ Naokazu Takeda,* and Tatsuo Miyamura***

Pig Liver Sausage as a Source of Hepatitis E Virus Transmission to Humans

**Philippe Colson,[1,2] Patrick Borentain,[3] Benjamin Queyriaux,[4,5] Mamadou Kaba,[1,2] Valérie Moal,[6] Pierre Gallian,[7] Laurent Heyries,[6] Didier Raoult,[1,2] and René Gerolami[2]**

[1]Pôle des Maladies Infectieuses et Tropicales Clinique et Biologique, Fédération de Bactériologie-Hygiène-Virologie, Centre Hospitalo-Universitaire Timone, [2]Unité de Recherche sur les Maladies Infectieuses et Tropicales Émergentes, Centre National de la Recherche Scientifique Unité Mixte de Recherche 6236–Institut de Recherche pour le Développement 3R198, Facultés de Médecine et de Pharmacie, Université de la Méditerranée (Aix-Marseille-II), [3]Service d'Hépato-Gastro-Entérologie, Centre Hospitalo-Universitaire Conception, [4]Institut de Veille Sanitaire, Cellule Interrégionale d'Epidémiologie Sud, [5]Institut de Médecine Tropicale du Service de Santé des Armées, Département d'Epidémiologie et Santé Publique, [6]Université de la Méditerranée, Assistance Publique des Hôpitaux de Marseille, Centre de Néphrologie et Transplantation Rénale, Hôpital Conception, and [7]Etablissement Français du Sang Alpes-Mediterranée, Marseille, France

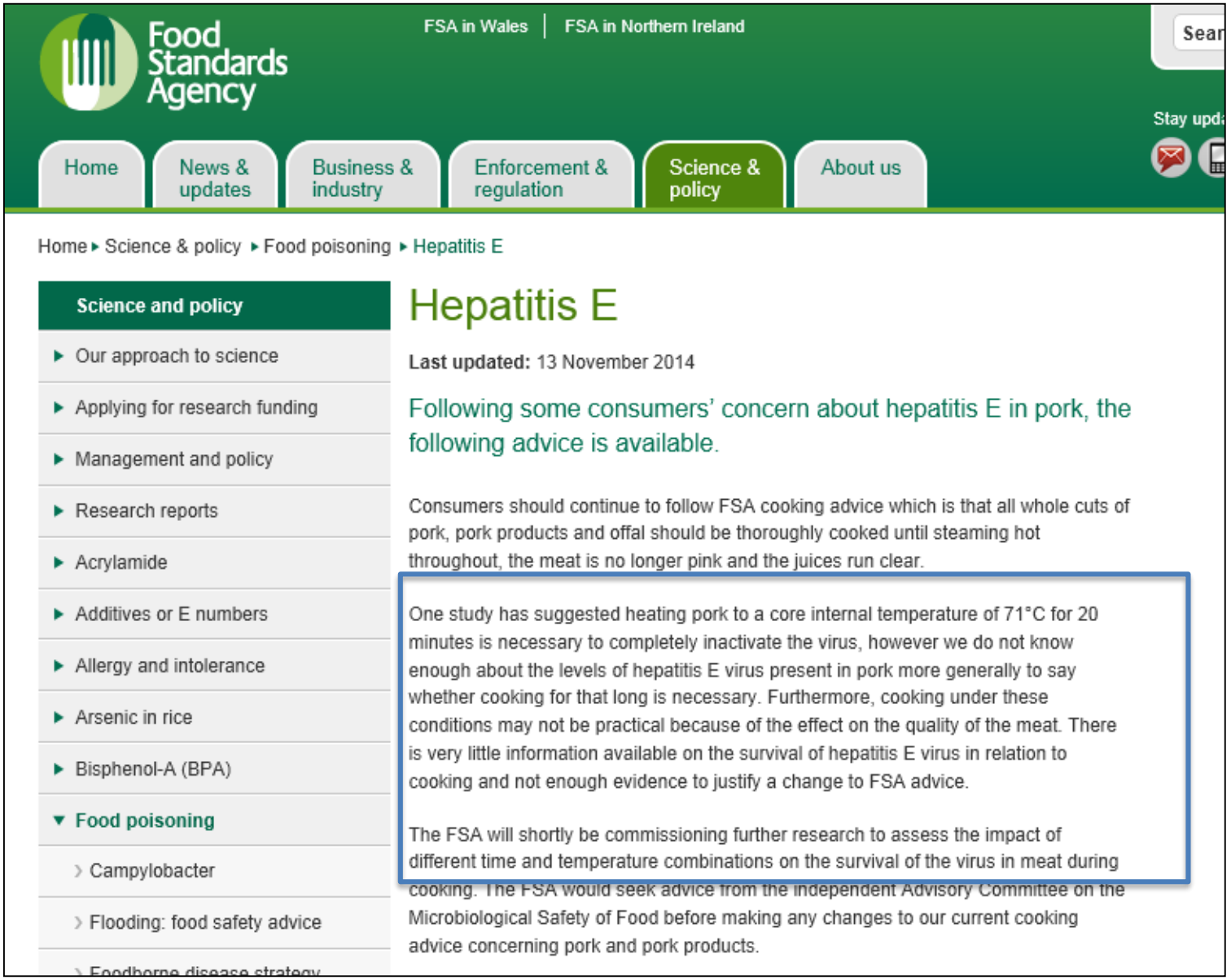
GCU Glasgow Caledonian University

University for the Common Good

# What foods have demonstrated detection of HEV?

- Pork Products
- Bivalve Molluscs
- Fruit
- Leafy vegetables

Is there evidence of infection via foodborne transmission?






Public health advice

# Control measures for HEV

Surrogates

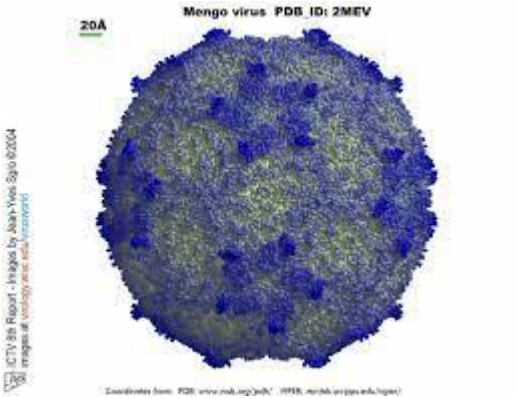
Diagnostics

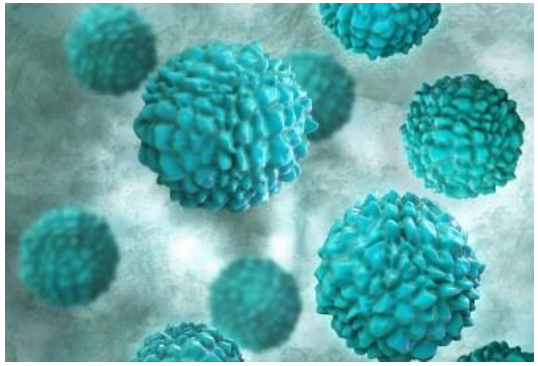
Thermal stability

Disinfection/Hygeine

Infectivity determination

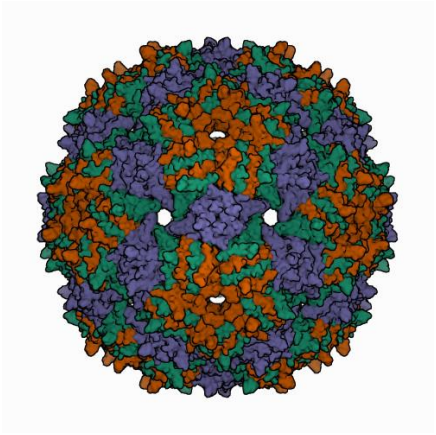
Risk

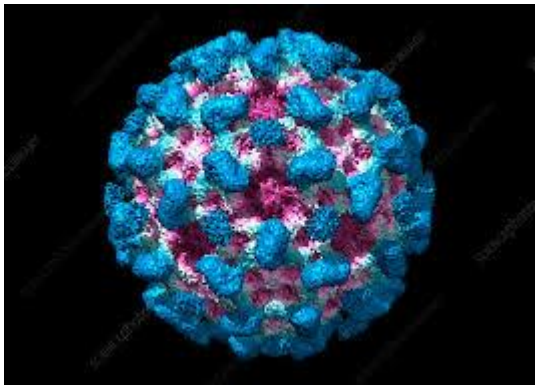


# Surrogates

# Do other viruses behave like HEV?





GCU Glasgow Caledonian University

University for the Common Good

# Control measures for HEV

Issues with current assays for diagnostics and beyond.

**Isolation and Extraction**

Adequate controls for extraction and detection

Need for SPCV suite for all assays

WHO HEV standard virus (sustainability)

**Detection**

Qualitative vs Quantitative

Infection linked to viral titre

Titres can be too low to quantify accurately

**Sensitivity and specificity**

**Costs**

# What is available for diagnostic detection of HEV?

Altona

http://www.altona-diagnostics.com/index.php/brealbstar-bhev-rt-pcr-kitb.html

Ceeram

http://www.ceeramtools.com/kit-hepatitis-e-virus-kit.html

Gensig -PrimerDesign™

http://www.genesig.com/products/9277


GCU Glasgow Caledonian University

University for the Common Good

# What else is available for diagnostics?

# ISO/TC 34/SC9/WG31

bsi. Inspiring trust for a more resilient world.

- Microbiology of the food chain: determination of hepatitis E virus in meat and meat products, and liver and liver products, using real-time RT-PCR

Inception meeting held on 12th January 2022

2nd meeting to be held on the 16th May
Santiago, Spain (ISFEV 2022)

GCU Glasgow Caledonian University

University for the Common Good

# Control measures for HEV

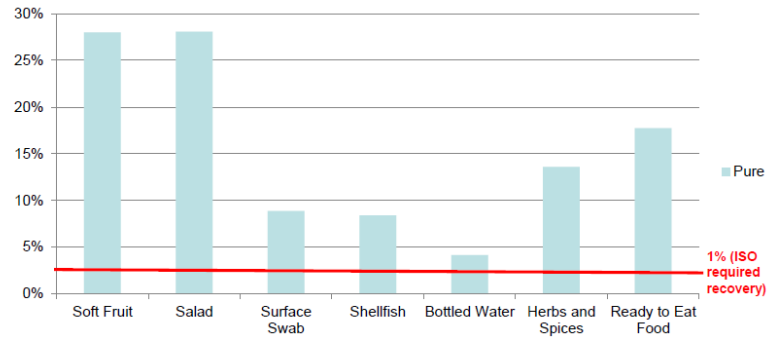
Issues with current assays for diagnostics and beyond.

Alternative assays?

Capsid integrity

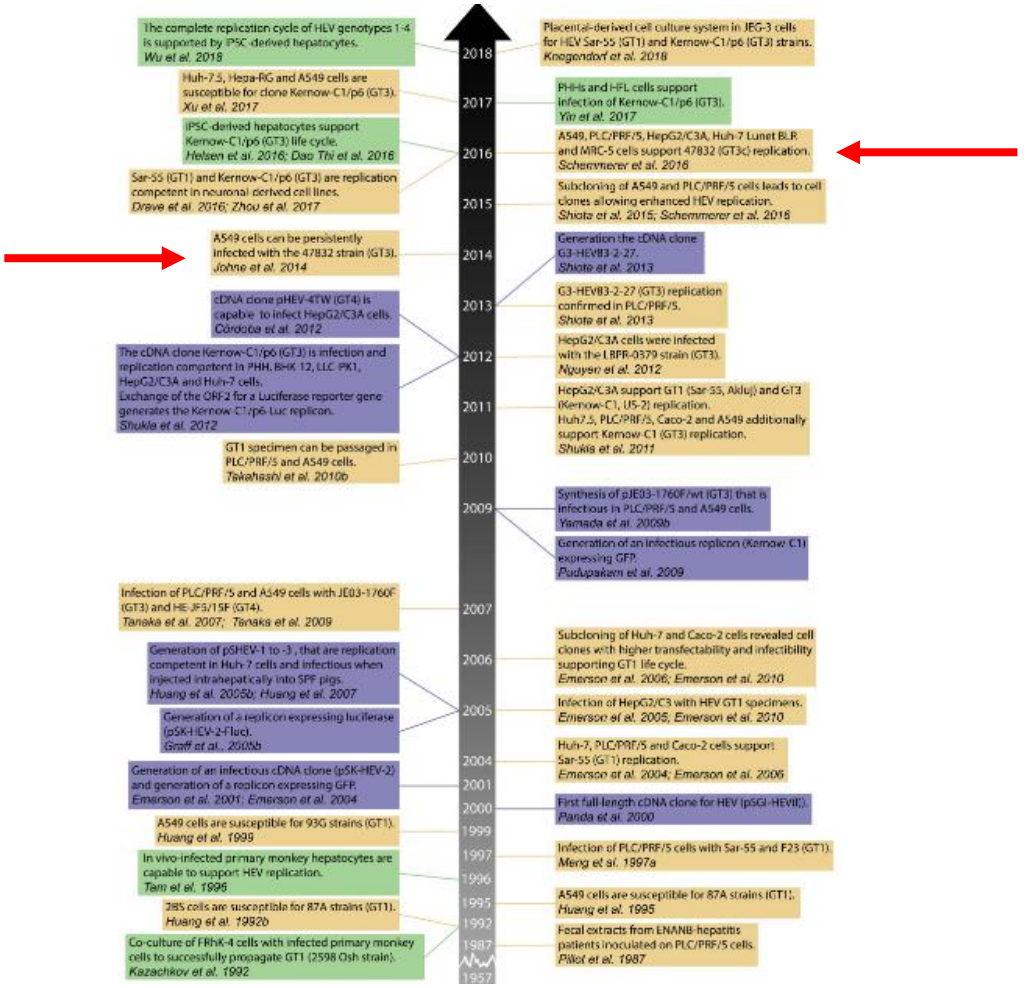
Ribo/Toehold switches

No consistent assay/detection system for infectious virus



# The problem with cell culture!

What is the difference between detection of NA and infection?




https://www.sciencedirect.com/science/article/pii/S016635421830720 4?via%3Dihub

# Outstanding issues

How do we test for infectious virus?

How much virus is infectious?

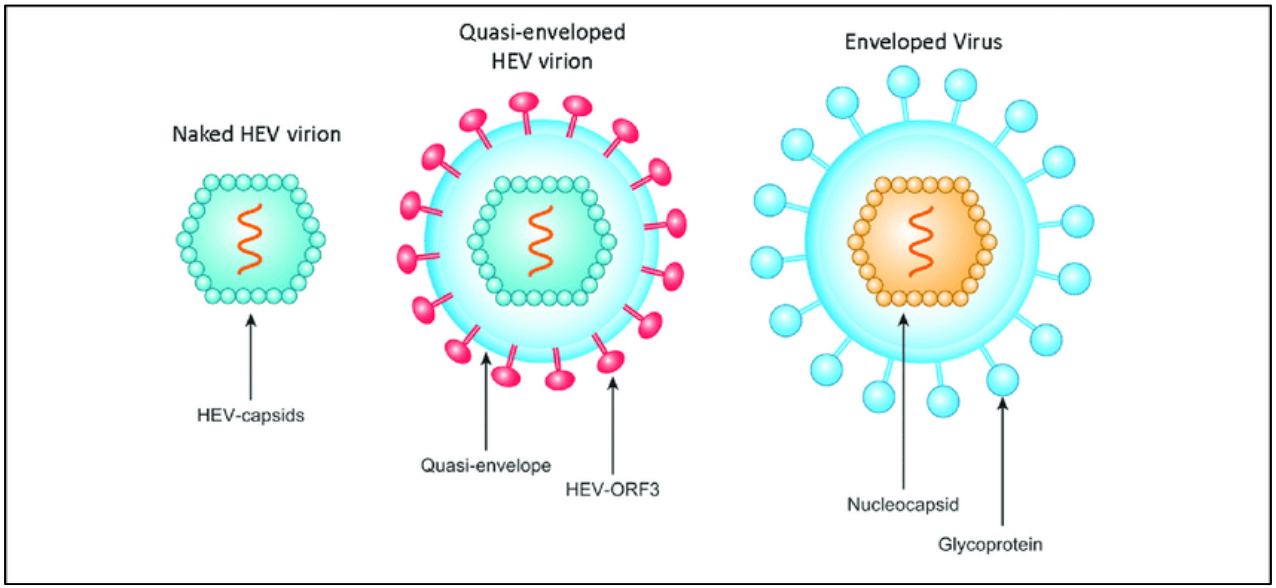
Does a food matrix affect viral replication?

What is the viral content of a food matrix and does this matter?

Figure removed as unpublished data

# Source origin of HEV

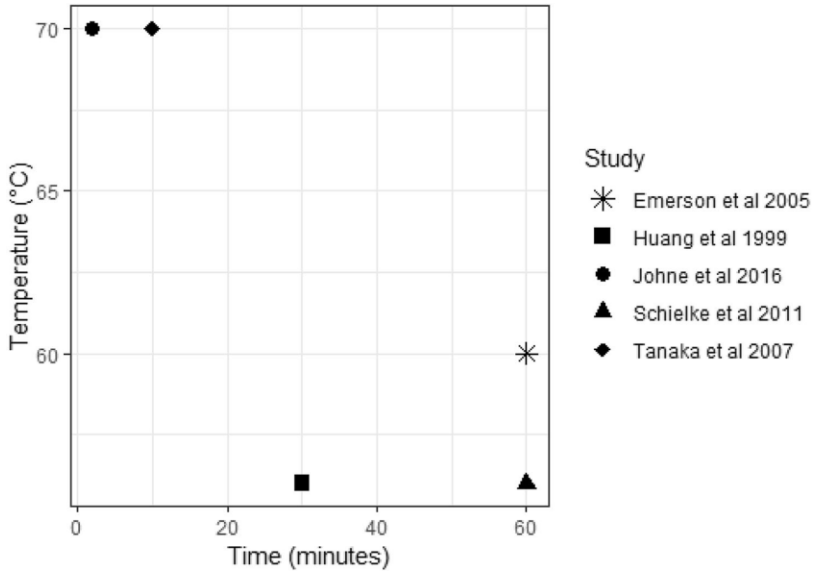
- Sera, Faeces, Liver, Cell culture.




What about quasi-envelope?

# HEV stability and susceptibility

- HEV inactivated at >71˚ C for 20 minutes
- Carbohydrate and fat composition of foods may contribute to thermal stability of HEV
- Unknown how long HEV can persist in the environment

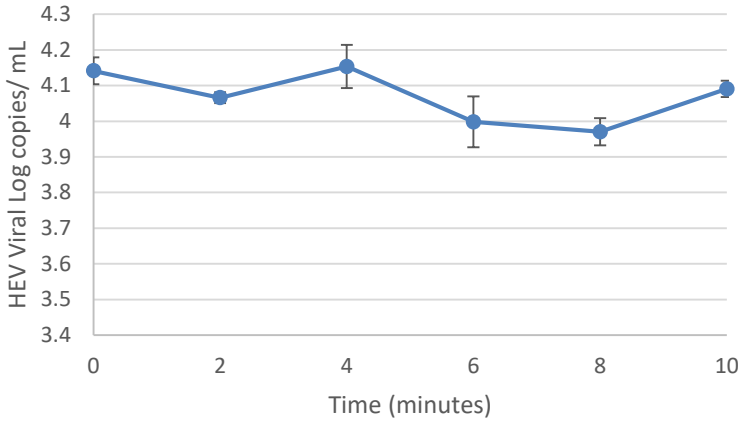



Thermal Inactivation of Infectious Hepatitis E Virus in Experimentally Contaminated Food

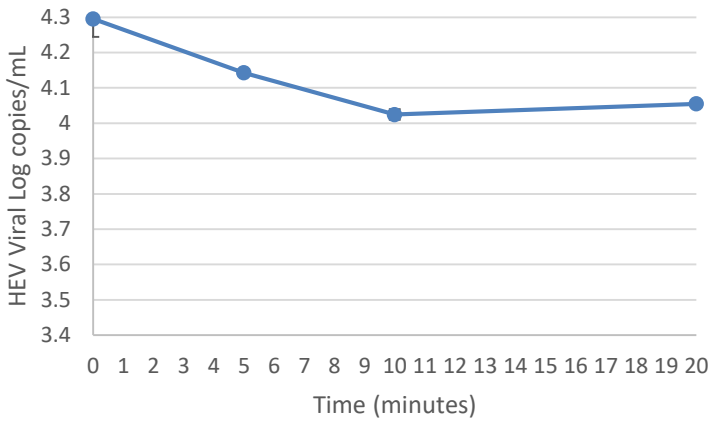
Elodie Barnaud,[a,b,c] Sophie Rogée,[a,b,c] Pascal Garry,[d] Nicolas Rose,[e] and Nicole Pavio[a,b,c]
UMR 1161 Virology, Anses, Laboratoire de Santé Animale, Maisons-Alfort, France[a]; UMR 1161 Virology, INRA, Maisons-Alfort, France[b]; UMR 1161 Virology, Ecole Nationale

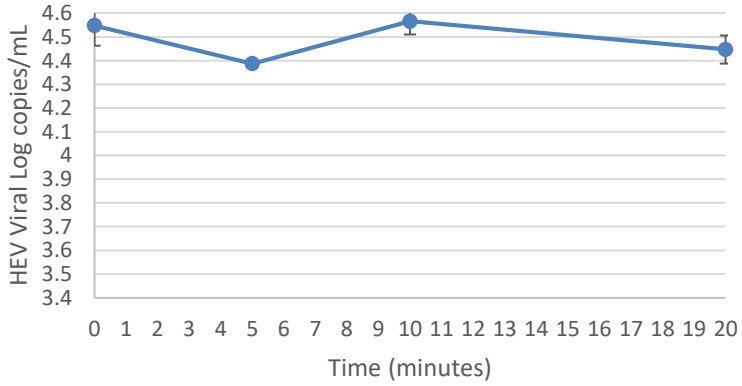
# Thermal Stability of HEV

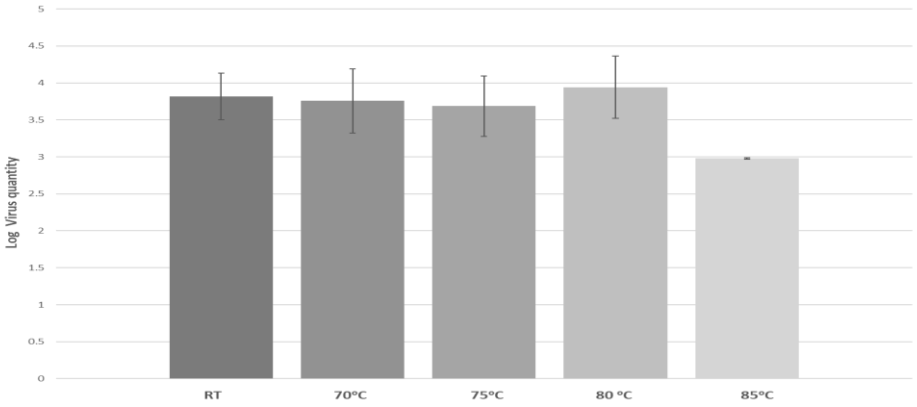
Serum




Cell culture



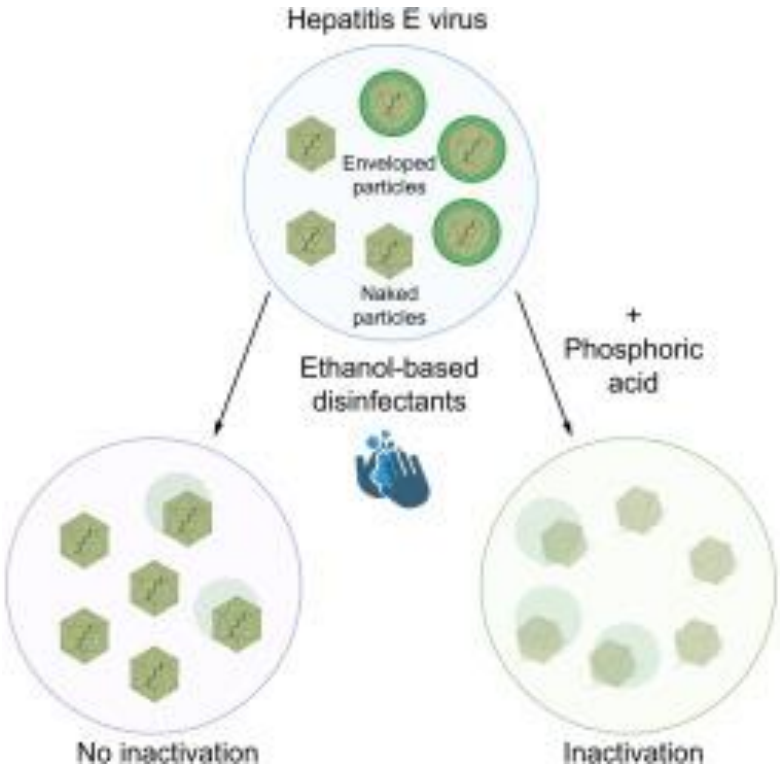

Faeces

Serum

≤ 1 log

# Disinfection/Hygiene

- Acid resistant – enhances stability
- Cold smoking does not eliminate virus
- Evidence of chlorine reducing viral titre in water sample
- Unknown how long HEV can persist in the environment




Behrendt et al; Journal of Hepatology 2022

Available online at www.sciencedirect.com
SCIENCE DIRECT®
Biochemical and Biophysical Research Communications 313 (2004) 67–73
BBRC
www.elsevier.com/locate/ybbrc
ELSEVIER

Acidic pH enhances structure and structural stability of the capsid protein of hepatitis E virus

# Joint FSA/EFSA workshop held in Feb 2016

Food Standards Agency

FSA in Wales | FSA in Northern Ireland

Search

Stay updated: Keep connected:

Home | News & updates | Business & industry | Enforcement & regulation | Science & policy | About us

Home ▸ News and updates ▸ News Centre ▸ Key priorities established for research on foodborne viruses

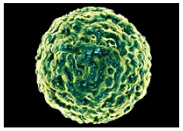
Accessibility | A A A

News and updates

- News centre
- Food alerts news
- Allergy alerts news
- Consultations
- Campaigns
- Help shape our policies

## Key priorities established for research on foodborne viruses

**Last updated:** 20 October 2016



How we tackle norovirus, hepatitis A and E viruses was the focus of a joint FSA/EFSA workshop that published its summary report today. The report identifies cross-cutting research themes, building on the first report of the FSA's Chief Scientific Advisor which highlighted that foodborne viruses have a significant impact on public health.

New research is now needed to measure the infectivity of norovirus and hepatitis A and E viruses – particularly in foods, the report concludes – and how the presence of norovirus in food relates to the public health risk is one of the top research priorities for scientists.

### Assessing the public health impact

The workshop, held at the Royal Society in London in February, brought together academics, virologist, clinicians, veterinarians, food industry specialists and regulators to consider public health impact from these viruses - and the feasibility of research to deliver benefits as the main criteria when deciding on the top research priorities.

Dr Paul Cook, FSA Head of Microbiological Risk Assessment, said: "Addressing these research areas identified by the experts at the workshop would make an important contribution to assessing as well as managing risk posed by these viruses in foodstuffs.

"This is a particular challenge for norovirus, which cannot be cultured in the laboratory despite many efforts to do so; hepatitis E virus has also proved difficult to culture."

### Shortlisting the research priorities

External sites

- The Summary Report of the Joint Scientific Workshop on Foodborne Viruses
  EFSA

The Food Standards Agency has no responsibility for the content of external sites

https://www.food.gov.uk/news-updates/news/2016/15612/key-priorities-established-for-research-on-foodborne-viruses

efsa

European Food Safety Authority

English (En)

Calendar

About | News | Discover | Science | Publications | Applications | Engage

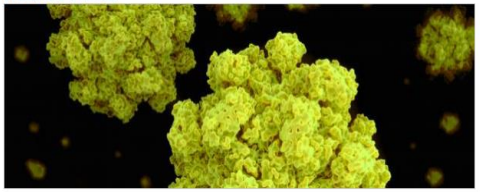
Home ▸ News ▸ Foodborne viruses: identifying research ne...

20 October 2016

Biological hazards

Corporate

## Foodborne viruses: identifying research needs to tackle public health risks



**EFSA has published a scientific report on the outcomes of a scientific workshop on foodborne viruses organised jointly by EFSA and the UK Food Standards Agency.**

The workshop took place earlier this year in London, and brought together academics, clinicians, veterinarians, food industry specialists and regulators with expertise in research, clinical settings and food producing/processing operations.

Against the background of an increasing number of outbreaks caused by foodborne viruses, the participants assessed the state of knowledge in this field. They focused on norovirus, the hepatitis A virus and the hepatitis E virus, which are of great public health concern in the EU. Knowledge gaps and research needs were identified and are summarised in the report.

The report, by the UK's Centre for Environment, Fisheries and Aquaculture Science (Cefas), also lists five priorities for further research.

The workshop was organised following a proposal to EFSA's Advisory Forum by the UK in 2015.

- Summary report of joint scientific workshop on foodborne viruses

Subject area

- Biological hazards
- Corporate

Related News

EFSA's fellowship initiative to increase Europe's risk assessment capacity
Corporate
published: 10 Nov 2016

Help us improve our website – complete this quick survey
Corporate
published: 07 Nov 2016

Chile and EFSA enhance cooperation in risk assessment
Corporate
published: 18 Oct 2016

Related

http://www.efsa.europa.eu/en/press/news/161020

GCU Glasgow Caledonian University

University for the Common Good

# Five main research priorities identified

The development and validation of direct and indirect methods for assessment of hepatitis E virus infectivity;

Establishing how the detection of norovirus in foodstuffs relates to public health risks;

Development of methods to evaluate norovirus and hepatitis A infectivity from food samples;

Development of standard methods and ISO methods for detection of hepatitis E virus in meat and meat products;

Establishing the burden of hepatitis E virus infections in humans in Europe.

# What are we still missing?

- The development and validation of direct and indirect methods for assessment of hepatitis E virus infectivity.
- Development of standard methods and ISO methods for detection of hepatitis E virus in meat and meat products.
- Establishing the burden of hepatitis E virus infections in humans in Europe.

Food Standards Agency
food.gov.uk

Campden BRI
food and drink innovation

JORVIK FOOD SAFETY SERVICES
HAVING TROUBLE TELLING YOUR HAZARDS FROM YOUR RISKS?
LET THE FOODSAFETYTEAM HELP.

# Thank you for your attention

Any questions?

GCU
Glasgow Caledonian University
University for the Common Good