

Hepatitis E virus update in Europe

The 28th IPFA/PEI Workshop
22nd September 2022, Porto, Portugal

Dr Heli Harvala
Consultant Medical Virologist and Principal Investigator
Microbiology Services, NHS Blood and Transplant
Colindale, UK

Honorary Associate Clinical Professor in Virology
UCL, Infection and Immunity, London, UK

heli.harvalasimmonds@nhsbt.nhs.uk



Sporadic hepatitis E

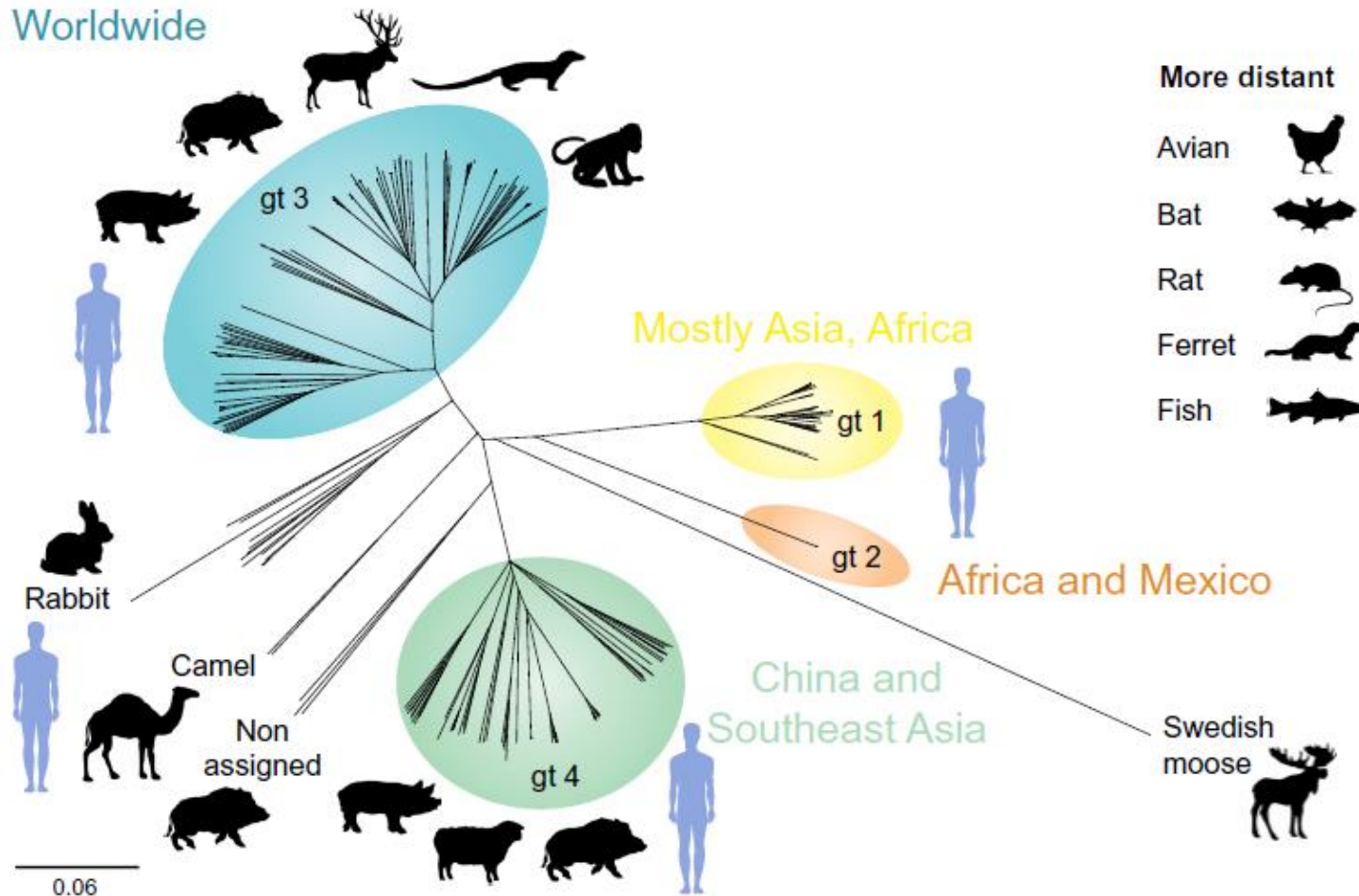
Blood donation screening

Lessons learnt from a clinical case

What's next?

Hepatitis E virus (species A)

Blood and Transplant



More distant

Avian



Bat



Rat



Ferret



Fish



Review



EASL JOURNAL OF HEPATOLOGY

Incubation period: 15 to 60 days

Update on hepatitis E virology: Implications for clinical practice

Yannick Debing^{1,†}, Darius Moradpour², Johan Neyts¹, Jérôme Gouttenoire^{2,*}

Features of endemic hepatitis E

- Caused by genotypes 1 and 2
- Large outbreaks in Africa and Asia
- Transmission: faecal-oral route, mostly waterborne
- Affects mostly young individuals: 15-35 years

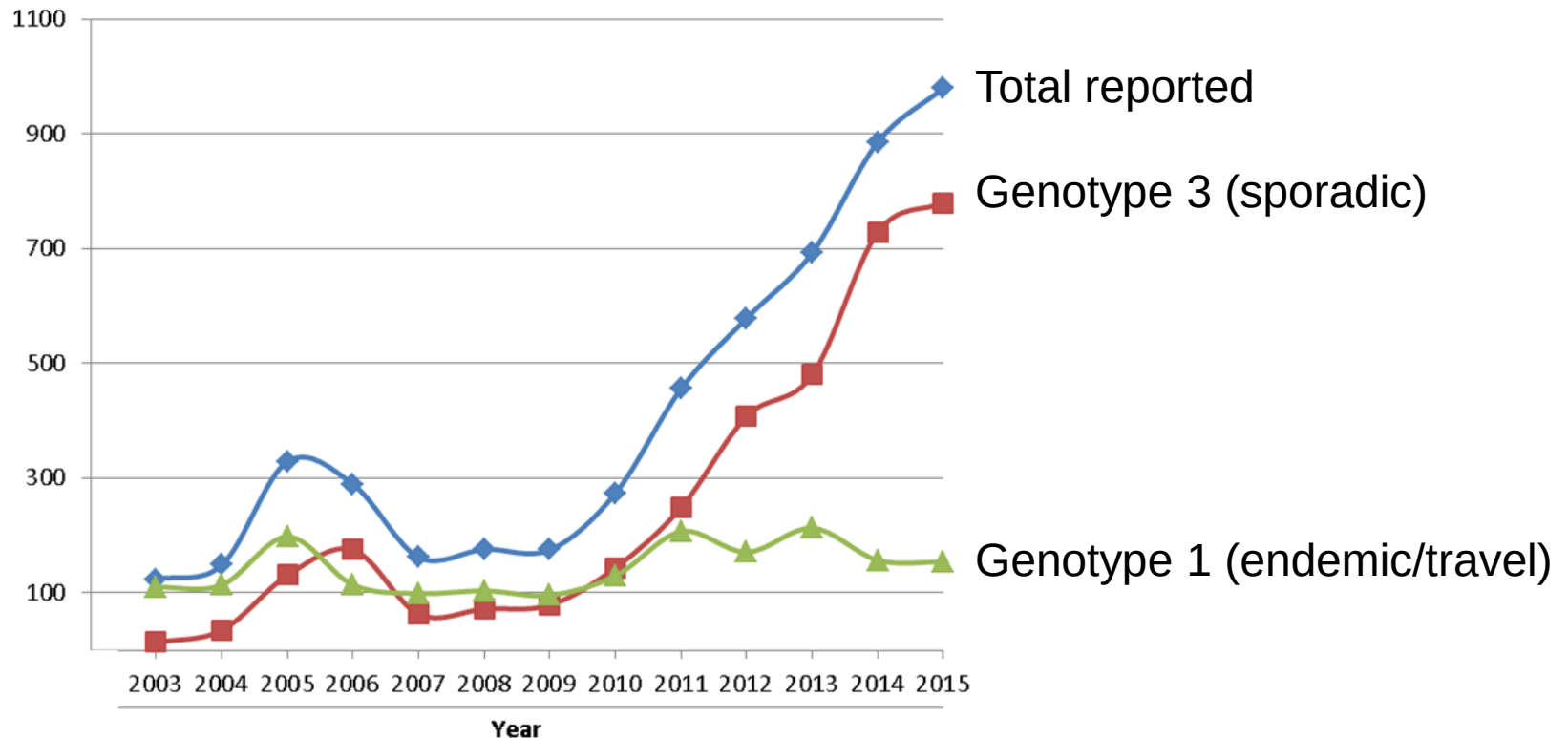


Features of sporadic hepatitis E

- HEV genotype 3 known to transmit via contaminated food, direct exposure to swine, blood transfusion and organ transplantation
- Often asymptomatic in healthy individuals
- Main cause of acute hepatitis and can lead to chronic-on-acute liver failure in those with underlying liver disease
- Immunosuppressed patients can fail to clear HEV infection and may develop chronic infection which can be very difficult to treat and can lead to cirrhosis



Sporadic hepatitis E in the UK



Public Health England (PHE) has been running a programme of enhanced surveillance for hepatitis E infection in the general population since 2003

TRANSFUSION

Transfusion-transmitted hepatitis E caused by apparently indigenous hepatitis E virus strain in Hokkaido, Japan

Keiji Matsubayashi✉, Yasuhiro Nagaoka, Hidekatsu Sakata, Shinichiro Sato, Kanji Fukai, Toshiaki Kato, Kazuaki Takahashi, Shunji Mishiro, Mitsunobu Imai, Naokazu Takeda, Hisami Ikeda

First published: 24 May 2004 | <https://doi.org/10.1111/j.1537-2995.2004.03300.x> | Cited by: 189



BACKGROUND: In industrialized countries, sporadic cases of hepatitis E have been reported in individuals who have never been in an endemic area. Hepatitis E virus (HEV) infection commonly occurs via the fecal-oral route but a potential risk of transfusion transmission route has been suggested.

STUDY DESIGN AND METHODS: A 67-year-old Japanese male patient who had never been abroad received a transfusion of blood from 23 voluntary donors and developed acute hepatitis with unknown etiology after transfusion. His blood samples were tested for viral markers of hepatitis viruses.

RESULTS: HAV, HBV, HCV, CMV, and EBV were ruled out as causative agents in this case. The patient's blood sample in the acute phase contained HEV RNA as well as IgM and IgG anti-HEV. HEV RNA was also detected in one of the FFP units transfused. The donor had no history of traveling abroad and had a normal ALT level at the time of donation. The PCR products from the patient and the donor showed complete identity for two distinct regions of HEV within open reading frame 1.

CONCLUSION: The patient was infected with HEV via transfused blood from a volunteer donor. A potential risk of posttransfusion hepatitis E should be considered even in nonendemic countries.



CrossMark

Hepatitis E virus in blood components: a prevalence and transmission study in southeast England



Patricia E Hewitt, Samreen Ijaz, Su R Brailsford, Rachel Brett, Steven Dicks, Becky Haywood, Iain T R Kennedy, Alan Kitchen, Poorvi Patel, John Poh, Katherine Russell, Kate I Tettmar, Joanne Tossell, Ines Ushiro-Lumb, Richard S Tedder

Summary

Background The prevalence of hepatitis E virus (HEV) genotype 3 infections in the English population (including blood donors) is unknown, but is probably widespread, and the virus has been detected in pooled plasma products. HEV-infected donors have been retrospectively identified through investigation of reported cases of possible transfusion-transmitted hepatitis E. The frequency of HEV transmission by transfusion and its outcome remains unknown. We report the prevalence of HEV RNA in blood donations, the transmission of the virus through a range of blood components, and describe the resulting morbidity in the recipients.

Methods From Oct 8, 2012, to Sept 30, 2013, 225 000 blood donations that were collected in southeast England were screened retrospectively for HEV RNA. Donations containing HEV were characterised by use of serology and genomic phylogeny. Recipients, who received any blood components from these donations, were identified and the outcome of exposure was ascertained.

Findings 79 donors were viraemic with genotype 3 HEV, giving an RNA prevalence of one in 2848. Most viraemic donors were seronegative at the time of donation. The 79 donations had been used to prepare 129 blood components, 62 of which had been transfused before identification of the infected donation. Follow-up of 43 recipients showed 18 (42%) had evidence of infection. Absence of detectable antibody and high viral load in the donation rendered infection more likely. Recipient immunosuppression delayed or prevented seroconversion and extended the duration of viraemia. Three recipients cleared longstanding infection after intervention with ribavirin or alteration in immunosuppressive therapy. Ten recipients developed prolonged or persistent infection. Transaminitis was common, but short-term morbidity was rare; only one recipient developed apparent but clinically mild post-transfusion hepatitis.

Interpretation Our findings suggest that HEV genotype 3 infections are widespread in the English population and in blood donors. Transfusion-transmitted infections rarely caused acute morbidity, but in some immunosuppressed patients became persistent. Although at present blood donations are not screened, an agreed policy is needed for the identification of patients with persistent HEV infection, irrespective of origin, so that they can be offered antiviral therapy.

Lancet 2014; 384: 1766–73

Published Online

July 28, 2014

[http://dx.doi.org/10.1016/](http://dx.doi.org/10.1016/S0140-6736(14)61034-5)

[S0140-6736\(14\)61034-5](http://dx.doi.org/10.1016/S0140-6736(14)61034-5)

See Comment page 1729

Transfusion Microbiology,

National Health Service Blood and Transplant, London, UK

(P E Hewitt FRCPATH,

S R Brailsford PhD, R Brett BSc,

S Dicks MSc, A Kitchen PhD,

P Patel MSc,

K I Tettmar MBA, J Tossell RN,

I Ushiro-Lumb FRCPATH,

Prof R S Tedder FRCPATH); Blood

Borne Virus Unit, Virus

Reference Department,

Microbiology Services

(S Ijaz PhD, S Dicks,

B Haywood BSc, P Patel,

J Poh PhD, K I Tettmar,

I Ushiro-Lumb, Prof R S Tedder)

and Centre for Infectious

Disease Surveillance and

Control (S R Brailsford,

I T R Kennedy MFPH,

K Russell MFPH), Public Health

England, London, UK; and

University College London,

Gower Street, London, UK

(Prof R S Tedder)

Timeline for hepatitis E screening

2012

- Reports of potential TTI cases to NHSBT increasing
- NHSBT/PHE HEV Prevalence and Transmission Study initiated

2014

- NHSBT/PHE HEV Study is published
- 1st SABTO HEV Working Group: HEV screened blood for tx recipients

2016

- NHSBT introduces partial blood donor screening in pools of 24
- 2nd SABTO HEV Working Group: Universal HEV RNA screening

Similar prevalence but different approach...

TABLE

Prevalence of hepatitis E virus RNA positive donations, population of transplanted patients at risk, reported cases of transfusion-transmitted hepatitis E virus and screening of blood donations in 11 European countries

Country	HEV RNA positive donations	Population at risk		Reported TT HEV infections	Screening of blood donations			
		allo-HSCT [51] AN (AR/p10mp)	SOT [52] AN (AR/pmp)		Implemented	Under Consideration	In evaluation	Not recommended
Denmark	1:2,331(2016) [16]	144 (201 – 300)	356 (63.6)					x
France	1:2,218 (2012–3) [18]	1,724 (201 – 300)	5,141(79.6)	x		x ^a		
Germany	1:1,241 (2012) [24]	2,892 (>300)	3,710 (44.9)	x		x ^b		
Greece	NA	169 (151 – 200)	171 (15.4)				x	
Ireland	1:2,778 (2016)	77(151 – 200)	246 (52.3)		x ^c			
Italy	NA	1,625 (201 – 300)	3,252 (53.2)				x	
The Netherlands	1: 726 (2016) [7]	1175 (>300)	1,315 (78.3)			x ^{d/e}		
Portugal	NA	137 (101 – 150)	739 (69.7)				x	
Spain	1:3,333 (2014) [53]	1,072 (201 – 300)	4,247 (90.2)	x			x	
Switzerland	NA	191 (201 – 300)	504 (61.5)			x		
United Kingdom	1:1,340–5,000 (2016)	1,602 (201 – 300)	4,561 (71.8)	x	x ^{o/f}			

Blood donation HEV screening

Different screening strategies from ID NAT to pooled testing; confirmatory testing often includes IgG and IgM; sequencing

- Ireland: ID NAT using Grifolds Panther
 - 95% LOD 7.9 IU/ml
- England: Pools of 24 using Roche
 - 95% LOD 18.6 IU/ml -> 446 IU/ml
- Scotland, Wales and Northern Ireland: Pools of 16 using Grifolds
 - 95% LOD 126.24 IU/ml

	Manufacturers claimed sensitivity ¹	Pool size (sensitivity in IU/ml)			
		ID	6	16	24
Grifols Panther	95% detection probability of 7.89 IU/ml (95% fiducial limits 6.63 - 9.83 IU/ml)	7.89	47.34	126.24	189.36
Roche 6800/8800	LoD of 18.6 IU/ml (95% CL15.9 - 22.6 IU/ml),	18.6	111.6	297.6	446.4

¹ using the WHO International Std for HEV

Case Study:

Donor with acute hepatitis E virus infection

- A regular apheresis platelet donor
- Donated in September 2019
 - HEV RNA detected at screening (tested in pools of 24)
 - HEV viral load of 4,900 IU/ml
 - HEV IgG and IgM antibodies not detected
 - Donor contacted; no symptoms at all
 - Invited for a repeat sample in 8 weeks

Is hepatitis E virus infection common in blood donors?

Blood donors and infections

Donor selection

- used to screen out people who may harm themselves or the blood supply if they donate
- leads to a low rate of infection in donors



Deferrals for individuals with high risk sexual behaviours reduced to **3 months** in November 2017

1.9 million donations tested • Positive donations discarded

HBV
63

HCV
39

HIV
6

Syphilis
54

HTLV
17

HEV
335

Recent infections

3 HBV **0** HCV **1** HIV



All transmission reported as sex between men and women

All recently infected individuals met donor selection rules

Recent infection used to model the risk of a testing miss

23 Syphilis



19

4

4 did not meet donor selection rules: 3 sex between men, 1 known infection

Recent syphilis indicates higher risk of other sexual infections



NHSBT only testing new and non-leucodepleted donations since January 2017

Review of testing showed that:

Most positive cases identified in new donors

HTLV lookback demonstrated efficacy of leucodepletion in reducing transmission risk



Universal HEV testing introduced

2017 vs 2016



80%
tested
0.02%
positive



30%
tested
0.04%
positive

Infection usually self limiting, may be more severe in immunosuppressed

Hepatitis E infected blood donors remain largely asymptomatic (n=146)

Symptom or clinical sign ^a	Before donation	Around donation	After donation
Fatigue	37	38	85
Joint pain/aches	9	4	22
Feeling ill	11	1	21
Nausea	7	1	20
Change in appetite	5	1	10
Abdominal pain	6	2	13
Fever	5	3	7
Vomiting	4	0	5
Dark urine	5	5	18
Jaundice	1	1	6

^a Donors could report multiple signs and symptoms, and at multiple time points.

Case Study:

HEV RNA-positive donation used

- Previous donation 3 weeks prior to index donation

Donation had tested negative for HEV RNA at pooled screening

Archive re-tested by individual NAT

HEV RNA detected with VL < 37 IU/ml

Date	HEV RNA	HEV IgG	HEV IgM	Comments
3 weeks prior	VL ~ 37 IU/ml	Negative	Negative	Archive (donation already used)
Index	VL 4,900 IU/ml	Negative	Negative	Index donation

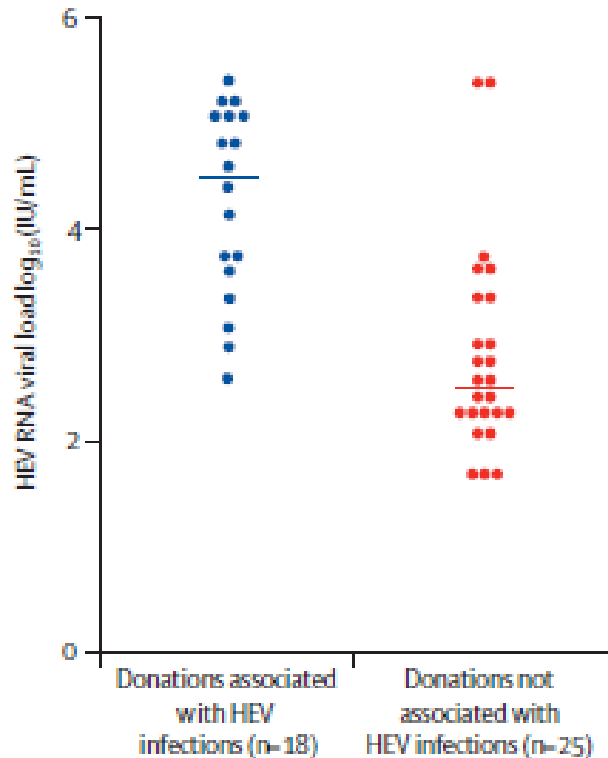
- Two recipients identified

50s with chronic disease but not immunosuppressed

40s with aplastic anaemia and portal hypertension

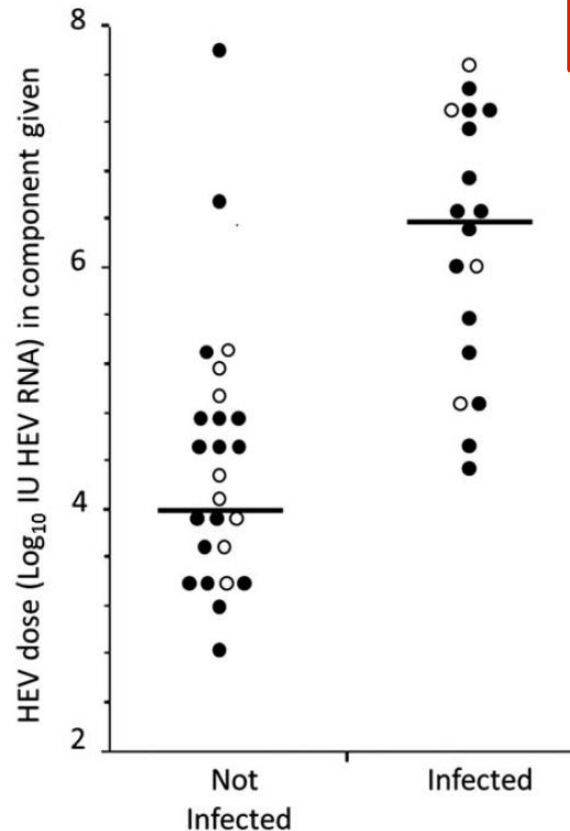
Does it matter? So little HEV RNA in this donations that we can hardly detect it...

How much is needed for transmission?



Hepatitis E virus in blood components: a prevalence and transmission study in southeast England

Patricia E Hewitt, Samreen Ijaz, Su R Brailsford, Rachel Brett, Steven Dicks, Becky Haywood, Iain T R Kennedy, Alan Kitchen, Poorvi Patel, John Poh, Katherine Russell, Kate I Tettmair, Joanne Tossell, Ines Ushiro-Lumb, Richard S Tedder



Hepatitis E risks: pigs or blood—that is the question

Richard S. Tedder,^{1,2,3} Samreen Ijaz,¹ Alan Kitchen,² Ines Ushiro-Lumb,² Kate I. Tettmair,² Patricia Hewitt,² and Nick Andrews⁴

Max dose here:
 $37\text{IU/ml} \times 180\text{ml} = \underline{6.660\text{IU}}$

Estimate: 20,000 IU would lead to transmission in 50% of recipients but two case reports where 7,000 IU and 9,000 IU transmitted (Huzly et al. 2013).

Lowest dose in French study ~10,000 IU noting that pathogen reduction did not eliminate the risk (Gallian et al., 2019).

Case Study:

Follow-up of recipients

- Recipient I with chronic disease but not immunosuppressed
 - no evidence of HEV infection after 6 months
- Recipient II with aplastic anaemia and portal hypertension
 - HEV RNA detected with VL 38,000 IU/ml two months after transfusion: close monitoring advised (*clinically well at the time!*)
 - Remained stable for a month; HEV VL peaked at 29,200,000 IU/ml and they were developing a good antibody response
 - This coincided with a sudden increase in bilirubin and ALT, hence patient was started on ribavirin
 - Their liver and renal function declined rapidly; he was admitted to ITU, not suitable for liver transplant and sadly the patient died
 - HEV transmission was confirmed by sequence analysis

What can we learn from this case?

- Would this case been identified as HEV infection if we would not have followed them up?
- Testing of asymptomatic recipients should be encouraged and include HEV RNA
- Infectious dose of HEV? Is it truly in plasma?
- Why recipient II died?
 - If he was cirrhotic, then acute-on-chronic liver failure could have been likely but this was reviewed and excluded...
 - How about aplastic anaemia and HEV?
 - Aplastic anaemia can follow HEV infection
 - Limited data on HEV infection on those with aplastic anaemia

	Primary diagnosis	Inferred immune suppression	Weeks to RNA positivity	Weeks to first detection of antibody	Duration of infection (weeks)*	Viral clearance	Alanine aminotransferase (IU/ml)	Comment
Patients 1–8								
Patient 1	Cardiac surgery	None	Marker not detected	8	NA	Yes	Not raised	No illness
Patient 2	Cardiac surgery	None	Marker not detected	14	NA	Yes	No information	No illness
Patient 3	Gastrointestinal bleeding	None	Marker not detected	6	NA	Yes	Not raised	No illness
Patient 4	Cardiac surgery	None	5	5	7	Yes	375, week 7	Mild jaundice
Patient 5	Sepsis	None	2	10	10	Yes	42, week 2	No information
Patient 6	Myelodysplastic syndrome	Mild	Marker not detected	6	NA	Yes	Not elevated	No illness
Patient 7	Myelodysplastic syndrome	Mild	Marker not detected	3	NA	Yes	No information	No information
Patient 8	Myelodysplastic syndrome	Mild	14	28	28	Yes	101, week 21	No information
Median for patients 1–8	..	..	5	7	10	..	..	..
Patients 9–14								
Patient 9	Aplastic anaemia	Moderate	8	Marker not detected	>12	No†	43, week 4	Sepsis death†
Patient 10	Metastatic cancer	Moderate	Marker not detected	6	NA	Yes	No information	No information
Patient 11	Aplastic anaemia	Moderate	4	10	>10	No†	200, week 7	Cardiac death†
Patient 12	Acute renal failure	Moderate	3	11	11	Yes	148, week 9	Steroid reduction
Patient 13	Non-Hodgkin lymphoma	Moderate	13	13	>43	No	No information	No information
Patient 14	Acute myeloid leukaemia	Moderate	12	21	25	Yes	1380, week 20	No information
Median for patients 9–14	..	..	8	11	18	..	..	..
Patients 15–18								
Patient 15	Acute myeloid leukaemia	High	17	38	>40	No	Not elevated	Deceased
Patient 16	Acute myeloid leukaemia	High	7	Marker not detected	16	Yes	Not elevated	11 weeks of Ribavirin
Patient 17	Failed transplant	High	7	Marker not detected	>10	No†	295‡, week 7	Sepsis death†
Patient 18	Multi organ transplant	High	11	37	44	Yes	40, week 22	Reduction of drug dose
Median for patients 15–18	..	..	9	37.5	30	..	..	..

Data are number, unless otherwise indicated. Median values are calculated from the numerator values in the table. NA=not applicable. *Period from transfusion to last detection of hepatitis E virus RNA; marked > when still viraemic after the end of follow-up. †Recipient died during follow-up, so relevant data excluded from numerical analysis. ‡Transaminitis thought to be secondary to abdominal sepsis and haematoma.

Table 3: Outcome in 18 recipients infected by transfusion of a blood component from a viraemic donor, ranked by immunosuppression

How often our donation screening fails to detect hepatitis E virus RNA?

	SCREENING		PREVIOUS DONATIONS		
Year	Apheresis donations screened	HEV RNA positive donations	Retrospective testing of previous donations	HEV RNA detected on re-testing	Components produced and supplied for clinical use
2016-2017	144027	44	35	2	4
2018	70709	24	24	3	6
2019	68907	14	14	2	4
2020	66680	24	25	2	4
Total	350323	108	98	9	18

Two cases of confirmed HEV transmission

Table 5. Details of lookback investigations into 9 HEV RNA positive platelet donations supplied for clinical use in England, March 2016 to December 2020*

Donation no.	HEV viral load, IU/mL†	Components	Recipient details	Recipient follow-up testing results
Donation 1	4	Platelet 1 Platelet 2	Hospitals informed, no data back	NA
Donation 2	8	Platelet 1 Platelet 2	Hospitals informed, no data back	NA
Donation 3	<37	Platelet 1 Platelet 2	Hospitals informed, no data back	NA
Donation 4	<37	Platelet 1 Platelet 2	Hospitals responded, no evidence of transmission	NA
Donation 5	37	Platelet 1 Platelet 2	M, 50–60 years, B-cell lymphoma F, 20–30 y, sepsis	<u>Confirmed transmission</u> Deceased
Donation 6	37	Platelet 1 Platelet 2	F, 60–70 y, aplastic anemia M, 50–60 y, lymphoma	Tested negative Tested negative
Donation 7	4.5	Platelet 1 Platelet 2	M, 40–50 y, aplastic anemia F, 50–60 y, vascular syndrome	<u>Confirmed transmission</u> Tested negative
Donation 8	10	Platelet 1 Platelet 2	M, 60–70 y, aplastic anemia M, <10 y, cancer	Tested negative Deceased
Donation 9	3	Platelet 1 Platelet 2	F, 40–50 y, myelodysplastic syndrome M, 40–50 y, acute myeloid leukemia	Tested negative Deceased

*Each donation was tested for HEV RNA and divided into 2 platelet packs.

†Estimated viral loads given where available. HEV, hepatitis E virus; NA, not applicable.

Estimated number of non-detections by pooled screened

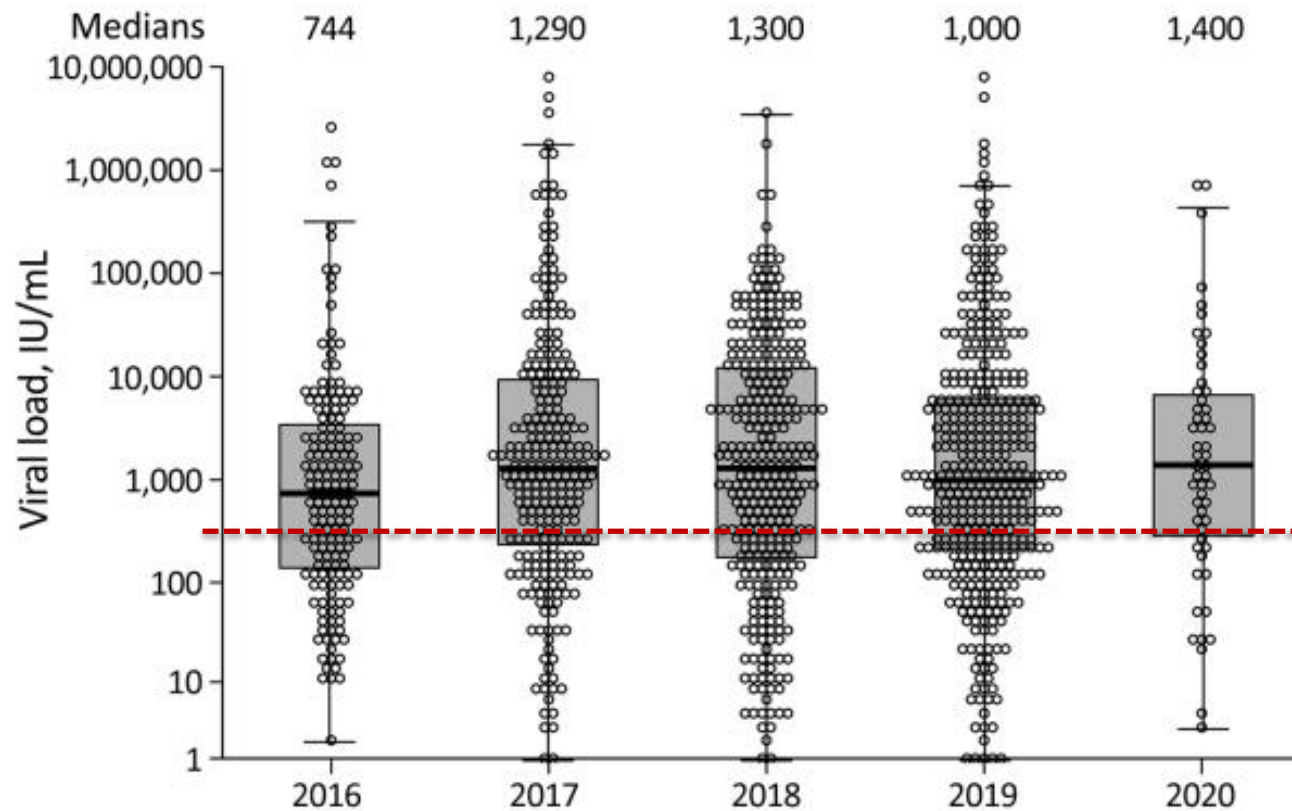
Table 3. Estimated number of hepatitis E virus RNA–positive donors not detected, according to 7-day window period risk for apheresis and whole blood donors, England, March 2016–December 2020

Donation type, year	Donations tested	No. not detected if window period 7 days (95% CI)
Apheresis		
2016	69,605	2.62 (1.68–3.90)
2017	74,422	2.19 (1.34–3.38)
2018	70,709	2.62 (1.68–3.90)
2019	68,907	1.64 (0.92–2.70)
2020	66,680	2.62 (1.68–3.90)
Total	350,323	11.70 (7.30–17.79)
Whole blood		
2016	413,153	19.02 (16.30–22.06)
2017	1,256,503	28.53 (25.17–32.21)
2018	1,488,808	38.36 (34.46–42.59)
2019	1,450,628	49.73 (45.27–54.52)
2020	1,338,489	41.42 (37.36–45.81)
Total	5,947,581	177.07 (158.55–197.19)

Harvala et al., *Emerging Infectious Diseases*, 2022

- The ratio of estimated maximum dose of HEV RNA in whole blood (25ml plasma) in comparison to platelets (180ml) is 1:7, and hence unlikely infectious (<1000 IU)
- All missed donations had viral load below 37 IU/ml and assay seems to be performing better than manufacturer says

Blood donation HEV screening in England: 37.5% of donations had viral load < 100 IU/mL

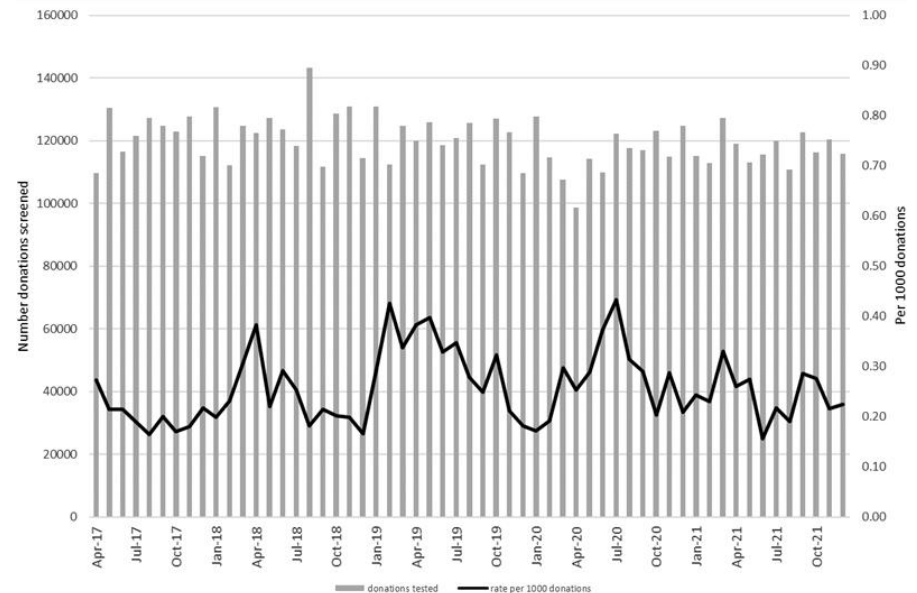
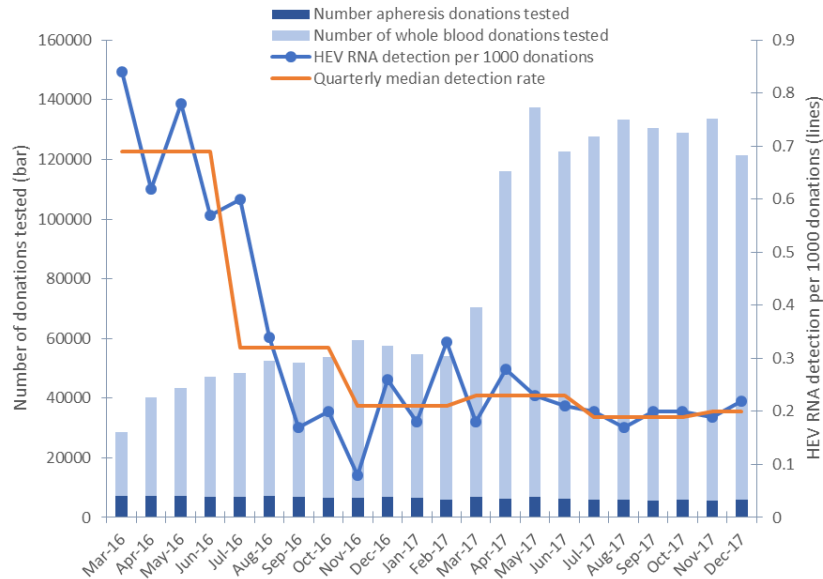


Is pooled screening good enough?

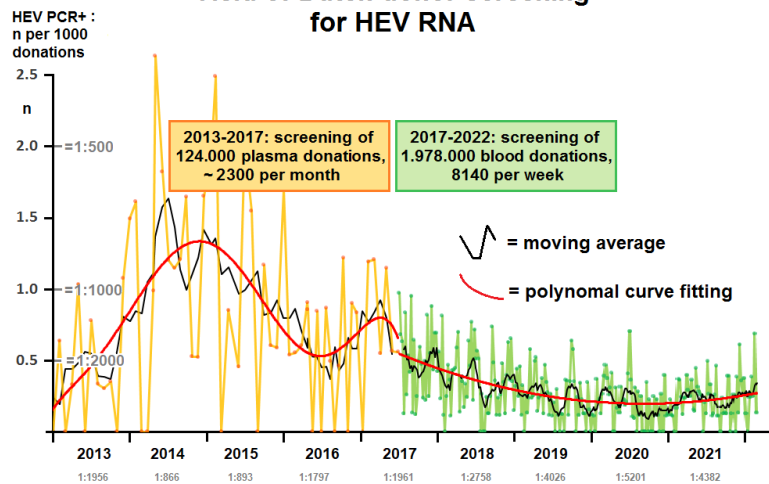
Kamp et al., (2018) proposed that pooled NAT screening is not sensitive enough as it would only result a decrease in transmissions from 1488 cases (no testing) to 279 cases (pool of 96) and 124 cases (pools of 24) and 14 cases if single donor testing is applied. Laperche et al., (2022) suggests that a maximum of 12 donations should be pooled to reach sensitivity around 240 IU/ml.

Year	HEV RNA detected	Number of donations screened	RNA detected per 1000 donations
2016 <i>(from the beginning of March)</i>	198	482,758	0.41
2017	334	1,330,925	0.21
2018 ★	422	1,559,517	0.27
2019 ☆ ★	552	1,842,283	0.30
2020	458	1,649,057	0.28
2021	398	1,719,630	0.23
Total	2,362	8,584,170	0.28

Do we need to continue HEV screening?



Yield of Dutch donor screening for HEV RNA



Although the prevalence of HEV RNA detection has decreased from 1:700~1:1400, it has now settled to 1:4000~1:5000 in the Netherlands and UK. But this still account to a number of HEV infections!

Note solvent/detergent-treated plasma can also transmit HEV (Gallian et al., 2020) and hence needs to be screened.

Hepatitis E will be an issue for blood services until the problem is solved with the pig farming and food industry.

'Brexit virus' feared in 10% of sausages

A strain of hepatitis E in imported meat is leaving thousands ill



“93% of British pigs are infected with HEV, with 6% producing enough virus to infect humans. 10% of pork imported from Europe has the HEV strain. Infection linked to pig farms in France, Holland, Germany and Denmark.”

The Sunday Times

What next?



First human case of rat hepatitis found in Hong Kong

28 September 2018

f Share



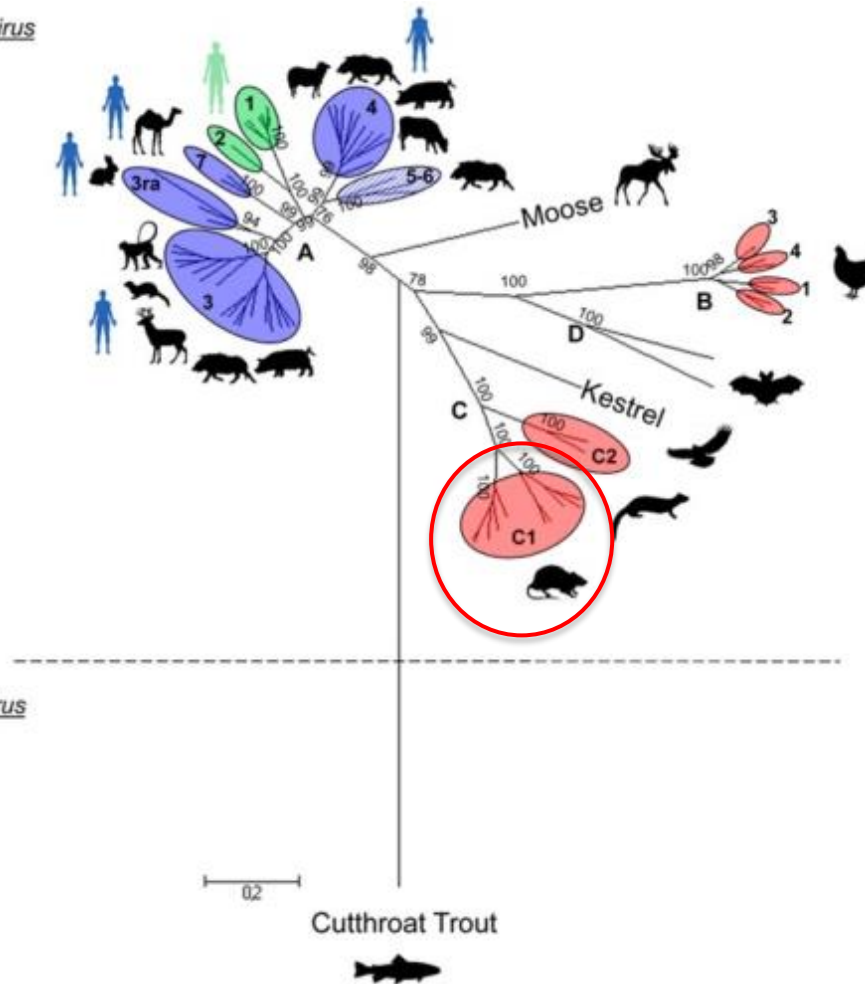
A 56-year-old man from Hong Kong has developed the world's first human case of rat hepatitis E.

Researchers say it is unclear how the man contracted the virus, but refuse bins outside his home were infested with rats.

Doctors discovered the case when tests on the man showed abnormal liver function following a liver transplant.

Rat hepatitis E virus in species C

Orthohepevirus



Piscihepevirus

Rat Hepatitis E Virus Linked to Severe Acute Hepatitis in an Immunocompetent Patient

Anton Andonov ✉, Mark Robbins, Jamie Borlang, Jingxin Cao, Todd Hatchette, Ashley Stueck, Yvon Deschambault, Kyle Murnaghan, Jessy Varga, Lynn Johnston

The Journal of Infectious Diseases, Volume 220, Issue 6, 15 September 2019, Pages 951–955, <https://doi.org/10.1093/infdis/jiz025>

Published: 14 January 2019 Article history ▼

“ Cite Permissions Share ▼

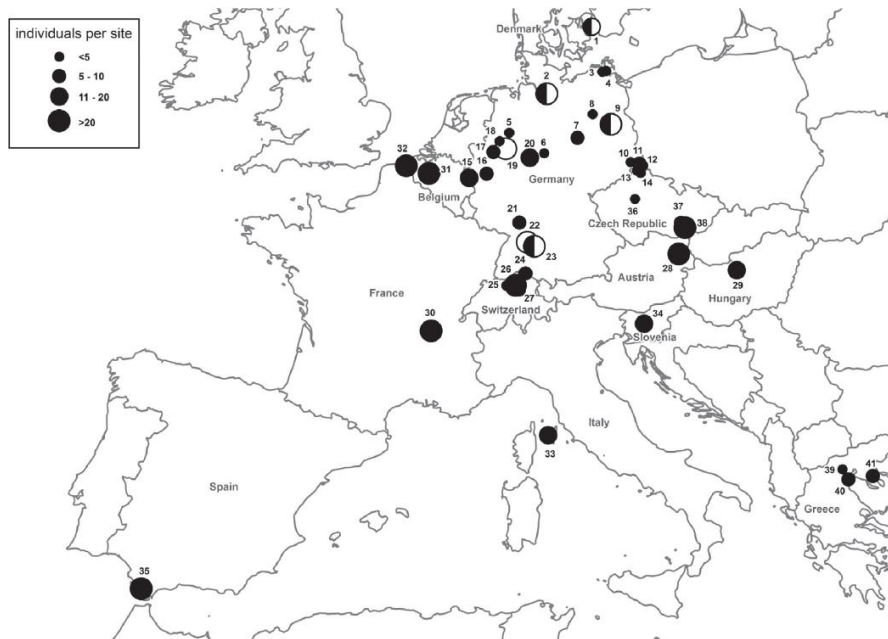
Abstract

Hepatitis E virus (HEV) is a major public health concern in developing countries where the primary transmission is via contaminated water. Zoonotic HEV cases have been increasingly described in Europe, Japan, and the United States, with pigs representing the main animal reservoir of infection. We report an unusual acute hepatitis infection in a previously healthy man caused by a rat HEV with a considerably divergent genomic sequence compared with other rat HEV strains. It is possible that rat HEV is an underrecognized cause of hepatitis infection, and further studies are necessary to elucidate its potential risk and mode of transmission.

Rat hepatitis E virus and Europe?

Detection of rat hepatitis E virus in wild Norway rats (*Rattus norvegicus*) and Black rats (*Rattus rattus*) from 11 European countries

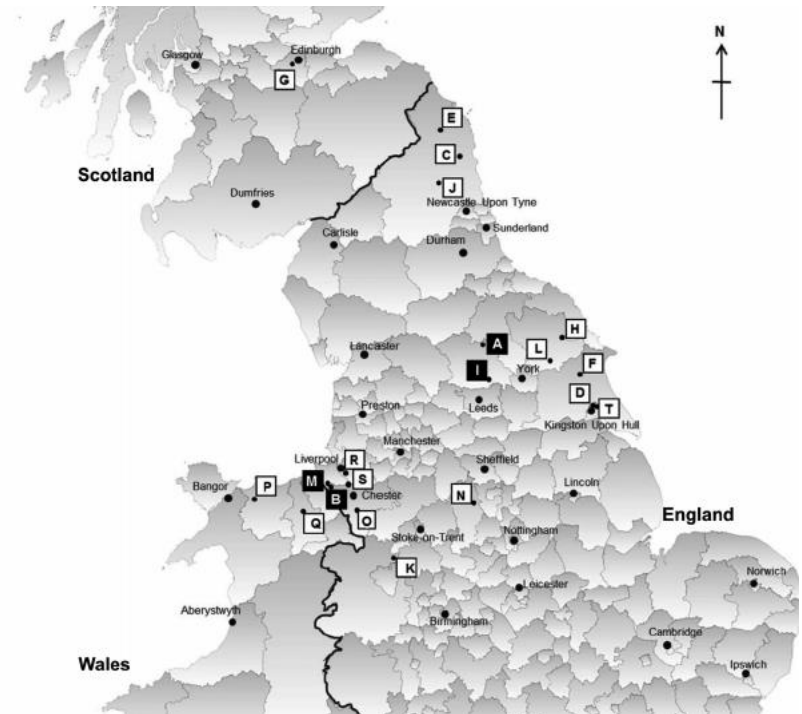
René Ryll^a, Samuel Bernstein^a, Elisa Heuser^a, Mathias Schlegel^{a,1}, Paul Dremsek^{a,2}, Maxi Zumpe^{a,3}, Sandro Wolf^{ab,4}, Michel Pépin^c, Daniel Bajomi^d, Gabi Müller^e, Ann-Charlotte Heiberg^f, Carina Spahr^g, Johannes Lang^h, Martin H. Groschup^a, Hermann Ansorgeⁱ, Jona Freise^j, Sebastian Guenther^k, Kristof Baert^l, Francisco Ruiz-Fons^m, Jiri Pikula^{n,o}, Nataša Knap^p, Ioannis Tsakmakidis^q, Chrysostomos Dovas^r, Stefania Zanet^s, Christian Imholt^t, Gerald Heckel^{u,v}, Reimar Johné^g, Rainer G. Ulrich^{a,w,*}



Veterinary Microbiology 208 (2017) 58–68

First detection of Hepatitis E virus (*Orthohepevirus C*) in wild brown rats (*Rattus norvegicus*) from Great Britain

Ellen G. Murphy^{1,2}  | Nicola J. Williams^{1,2} | Daisy Jennings³ | Julian Chantrey⁴ | Ranieri Verin⁴ | Sylvia Grierson⁵ | Lorraine M. McElhinney^{1,3} | Malcolm Bennett⁶



Zoonoses Public Health. 2019;66:686–694.

Rat hepatitis E virus infects humans

Table 2. Demographic and Clinical Characteristics of Immunocompromised Persons Diagnosed With Hepatitis E

Sridhar et al., CID 2022.

Characteristic	HEV-C1 Group (n = 9)	HEV-A Group (n = 12)
Sex, male	7 (77.8)	9 (75)
Mean age, y	59.8	52.8
Immunosuppressive condition		
Liver transplant	2 (22.2)	1 (8.3)
Kidney transplant	3 (33.3)	6 (50.0)
Heart transplant	0 (0.0)	1 (8.3)
Lung transplant	0 (0.0)	1 (8.3)
HSCT	1 (11.1)	1 (8.3)
Hematological malignancy	1 (11.1)	2 (16.7)
Advanced HIV	1 (11.1)	0 (0.0)
Rheumatic disorder	1 (11.1)	0 (0.0)
Hepatitis E outcomes		
Spontaneous resolution	1/9 (11.1)	0/12 (0.0)
Early ribavirin with SVR ^a	1/9 (11.1)	2/12 (16.7)
Persistent infection	7/9 (77.8)	10/12 (75.0)
Outcomes of persistent hepatitis E		
Death before treatment	2/7 (28.6)	2/10 (20.0)
Resolved with reduced immunosuppression	0/7 (0.0)	1/10 (10.0)
SVR on ribavirin	4/7 (57.1)	4/10 (40.0)
Ribavirin nonresponder	0/7 (0.0)	2/10 (20.0)
Responsive, but not attained SVR at time of study	1/7 (14.3)	1/10 (10.0)

Data are presented as No. (%) unless otherwise indicated.

Abbreviations: HEV, hepatitis E virus; HEV-A, *Orthohepevirus* species A; HEV-C1, *Orthohepevirus* species C, genotype 1; HIV, human immunodeficiency virus; HSCT, hematopoietic stem cell transplant; SVR, sustained virological response.

^aEarly ribavirin refers to ribavirin treatment before documentation of 3 months of viremia/hepatitis.

3 domestic cases identified in Spain by screening of 267 patients with acute hepatitis – none of them with known exposure to rodents, wild or domestic animals. Rivero-Juarez et al., 2022.

Remember – you will only find what you are looking for!



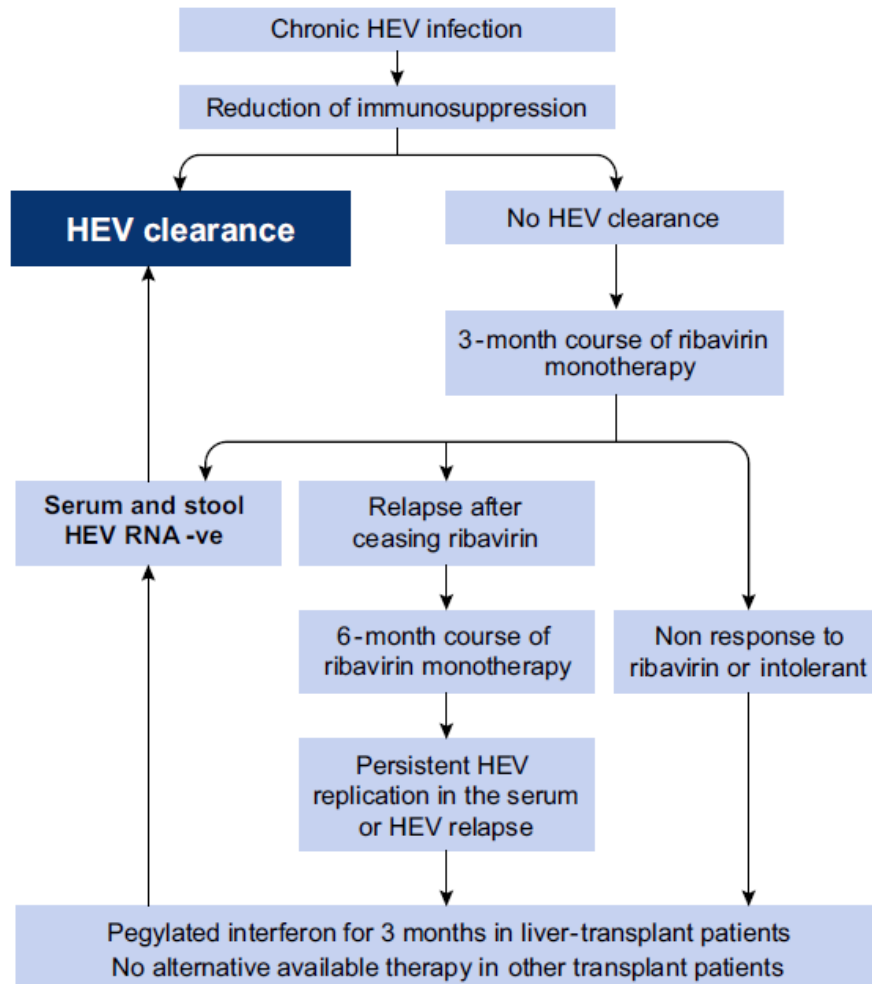
Thank you!

Blood and Transplant



EASL Clinical Practice Guidelines on hepatitis E virus infection[☆]

European Association for the Study of the Liver*

**Recommendations**

- Patients with abnormal LFTs after receiving blood products should be tested for HEV. **(A1)**
- EASL recommends that blood donor services screen blood donors for HEV by NAT, informed by local risk-assessment and cost-effectiveness studies, both of which may vary considerably by geographical location. **(A1)**

Recommendations

- EASL recommends decreasing immunosuppression at diagnosis of chronic HEV infection in solid organ transplant recipients, if possible. **(B1)**
- In patients with persisting HEV replication three months after detection of HEV RNA, EASL recommends ribavirin monotherapy for a duration of 12 weeks. **(B1)**
- At the end of the scheduled period of therapy, HEV RNA should be assessed in the serum and in the stool **(B1)**. If HEV RNA is undetectable in both, EASL suggests stopping ribavirin. **(C2)**