In The name of GOD

Hepatitis E Virus

An underestimated virus

Epidemiology, diagnosis, and treatment

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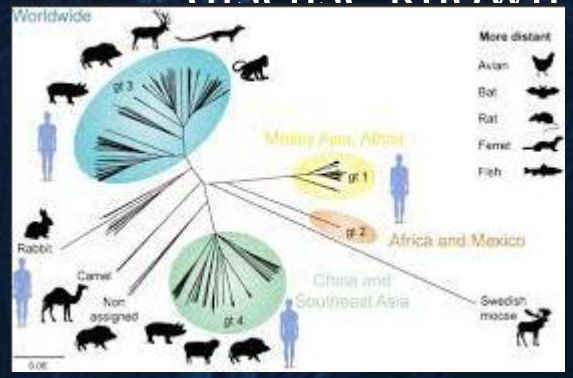
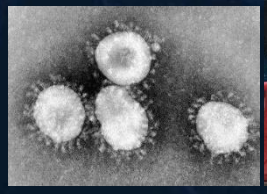
Introduction

- Recently, viral infectious diseases have threatened global public health safety.
- Major incidences of these emerging and re – emerging viral infectious diseases have a zoonotic link from arthropods, wild animals, domestic animals, and poultry.
- However, most of the emerging viral infectious diseases are caused by RNA viruses.
- Hepatitis E virus (HEV) is one such RNA virus causing the disease known as hepatitis E.





Introduction

- However, despite these alarming figures, hepatitis E is still grossly underestimated.
- There is poor awareness of the disease among physicians. Thus, routine check for the disease is rarely conducted in the hospitals in most parts of the world.
- Thereby leading to misdiagnosis and under diagnosis of hepatitis E.

Introduction

- There is also a paucity of research on the epidemiology of the disease, particularly in developed countries.
- This is due to the initial idea that hepatitis E is only endemic in the developing regions of the world.

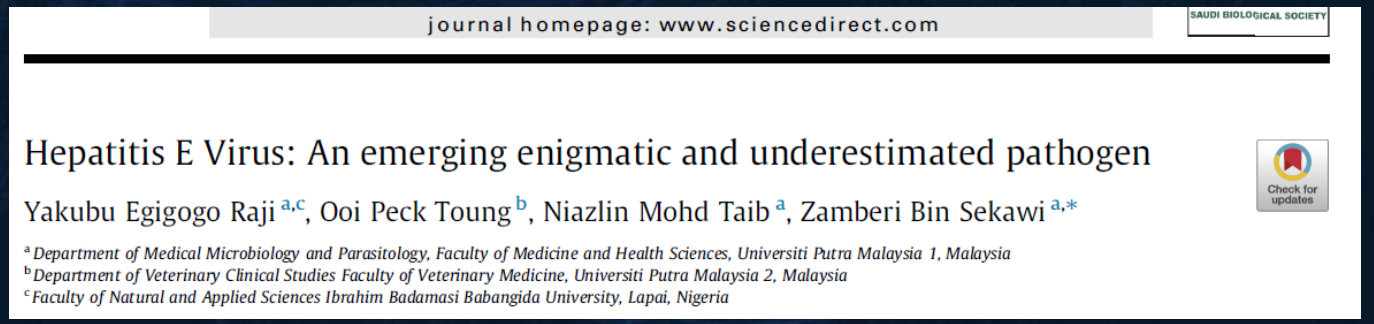
Review

Hepatitis E: an emerging infection in developed countries

Harry R Dalton, Richard Bendall, Samreen Ijaz, Malcolm Banks

Lancet Infect Dis 2008; 8: 698–709

Hepatitis E is endemic in many developing countries where it causes substantial morbidity. In industrialised countries, it is considered rare, and largely confined to travellers returning from endemic areas. However, there is now a growing



journal homepage: www.sciencedirect.com

SAUDI BIOLOGICAL SOCIETY

Hepatitis E Virus: An emerging enigmatic and underestimated pathogen

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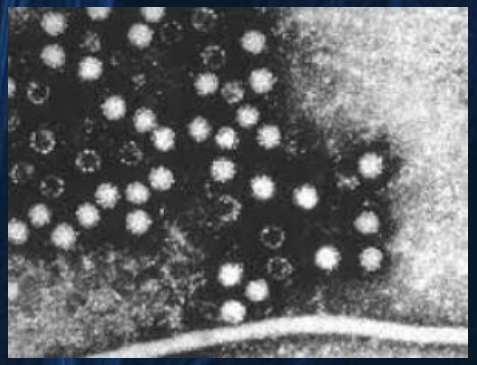
[c] Faculty of Natural and Applied Sciences Ibrahim Badamasi Babangida University, Lapai, Nigeria

Check for updates

HEV history

- A large outbreak of jaundice that occurred in New Delhi
- India between 1955 and 1956, was due to an enterically transmitted non-A non-B hepatitis

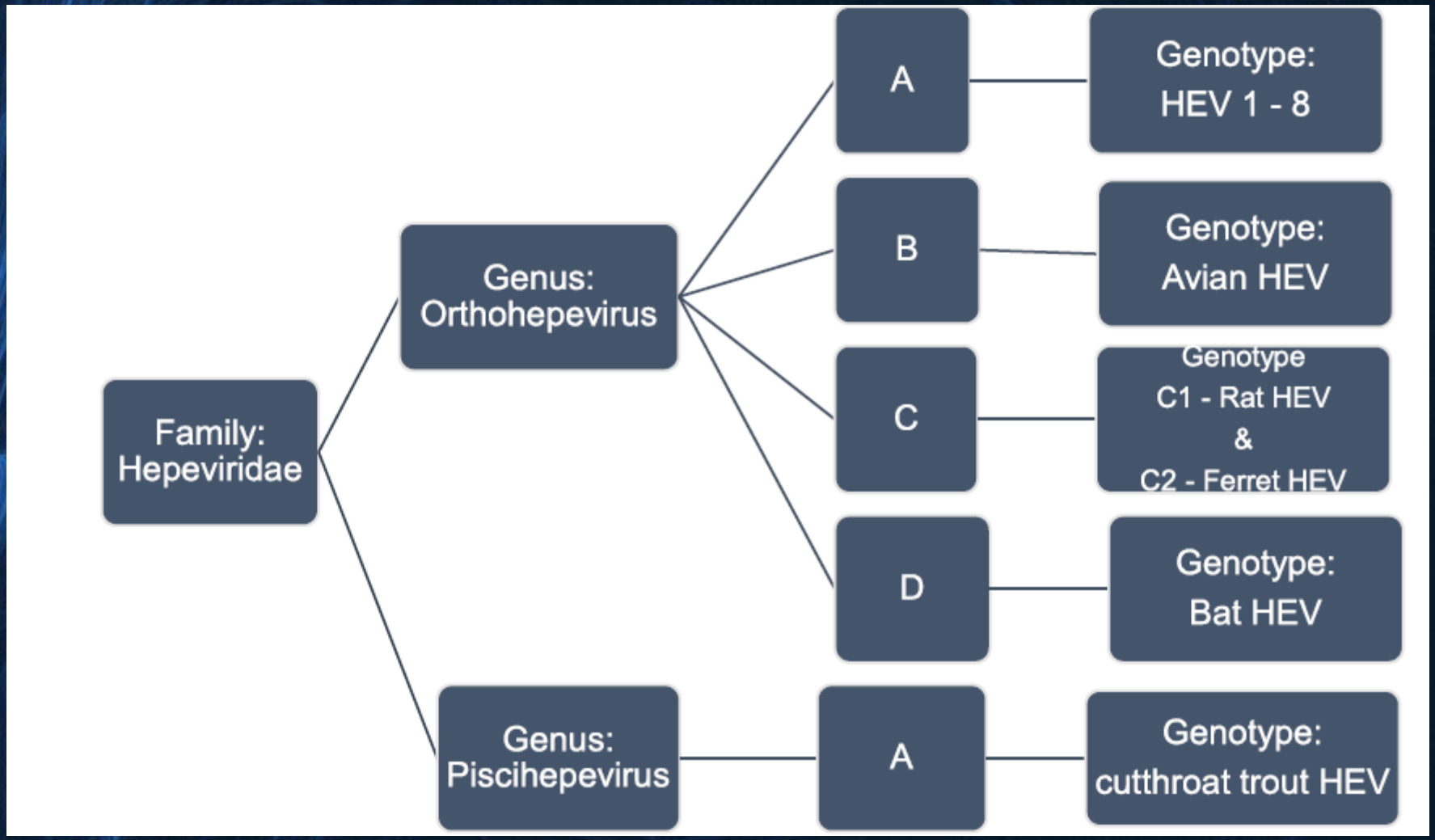
- In 1980, Khuroo suggested that the causative agent of an outbreak of non-A, non-B acute viral hepatitis that occurred in 1978 in the Kashmir valley of India was likely enterically transmitted

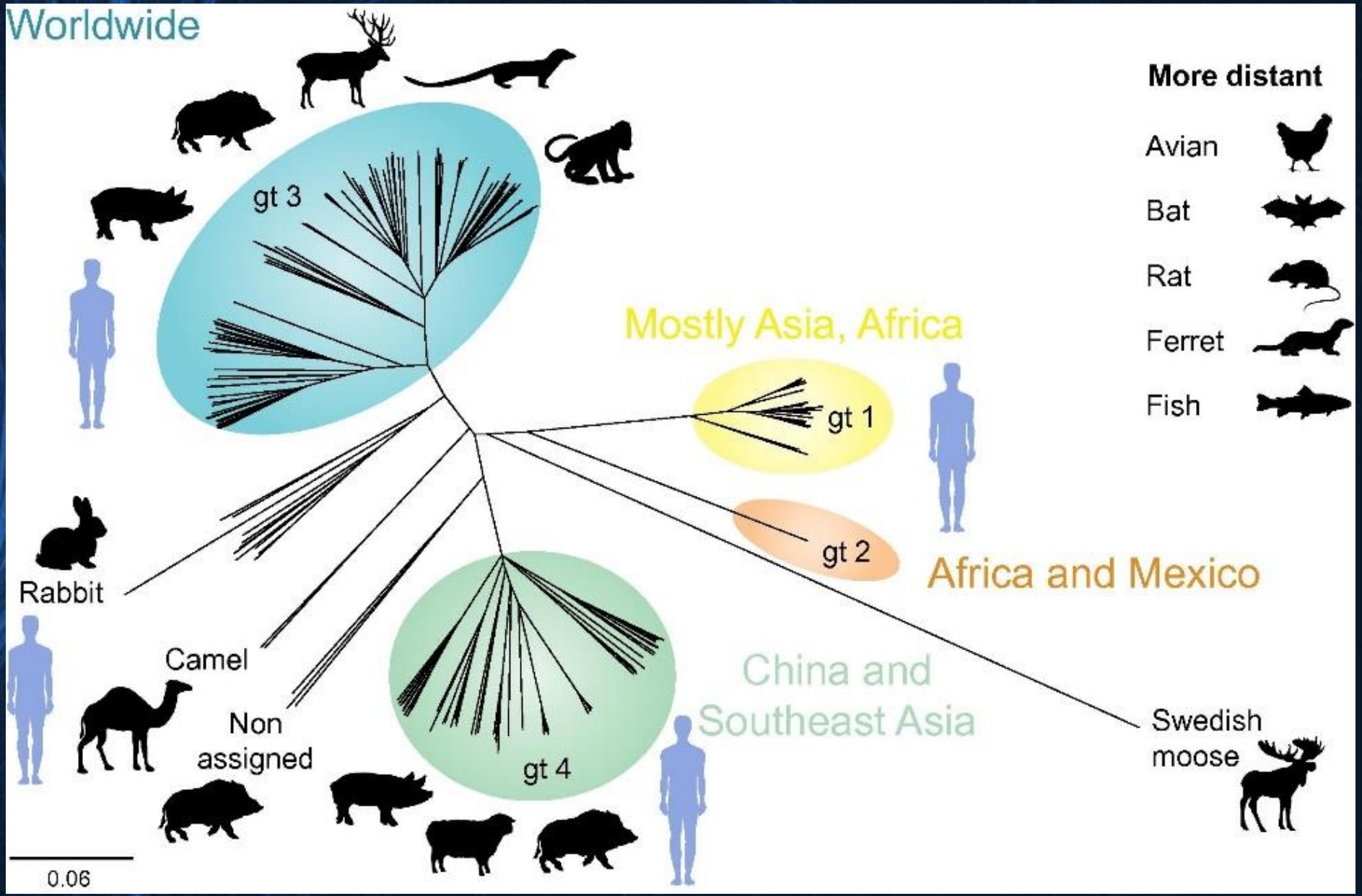


1980	Description of epidemic NANB hepatitis Khuroo MS
1981	Association of hepatitis E with pregnancy Khuroo et al
1983	Acute sporadic hepatitis and NANB hepatitis Khuroo et al
1983	Transmission/visualization of VLPs Balayan et al
1987	Serial animal passage and physicochemical properties of VLPs Bradley et al
1990	Molecular cloning and sequencing of viral genome Reyes et al
1992	ELISA for HEV antibodies Yarbough et al

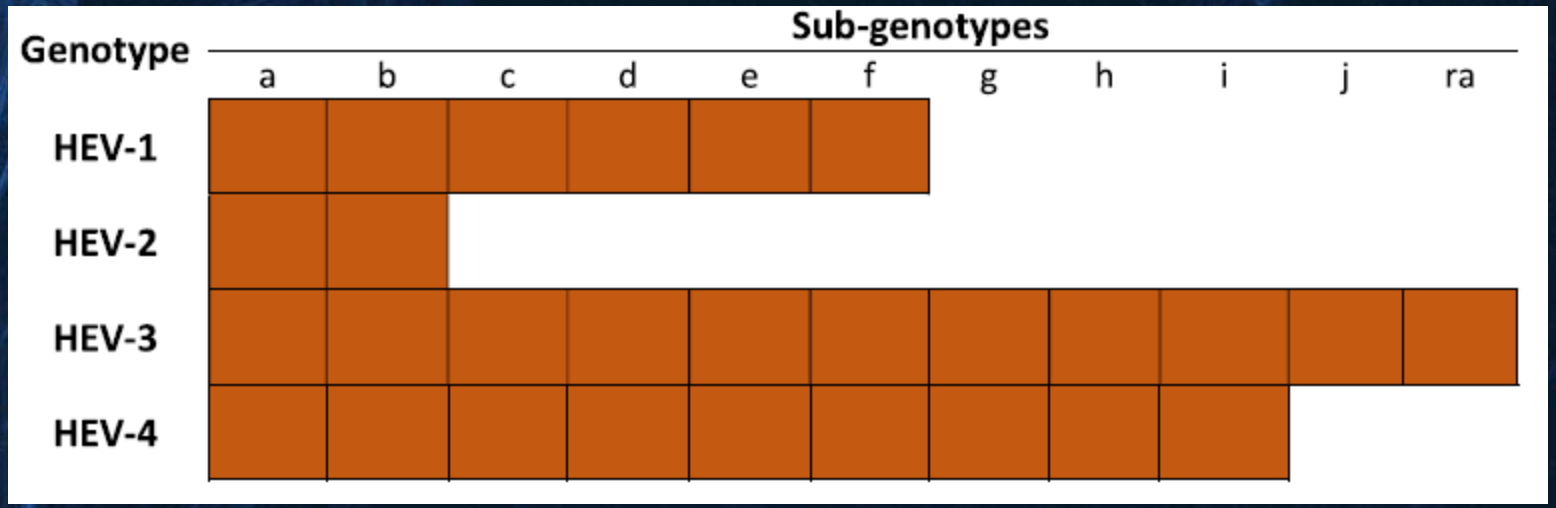
HEV Taxonomy

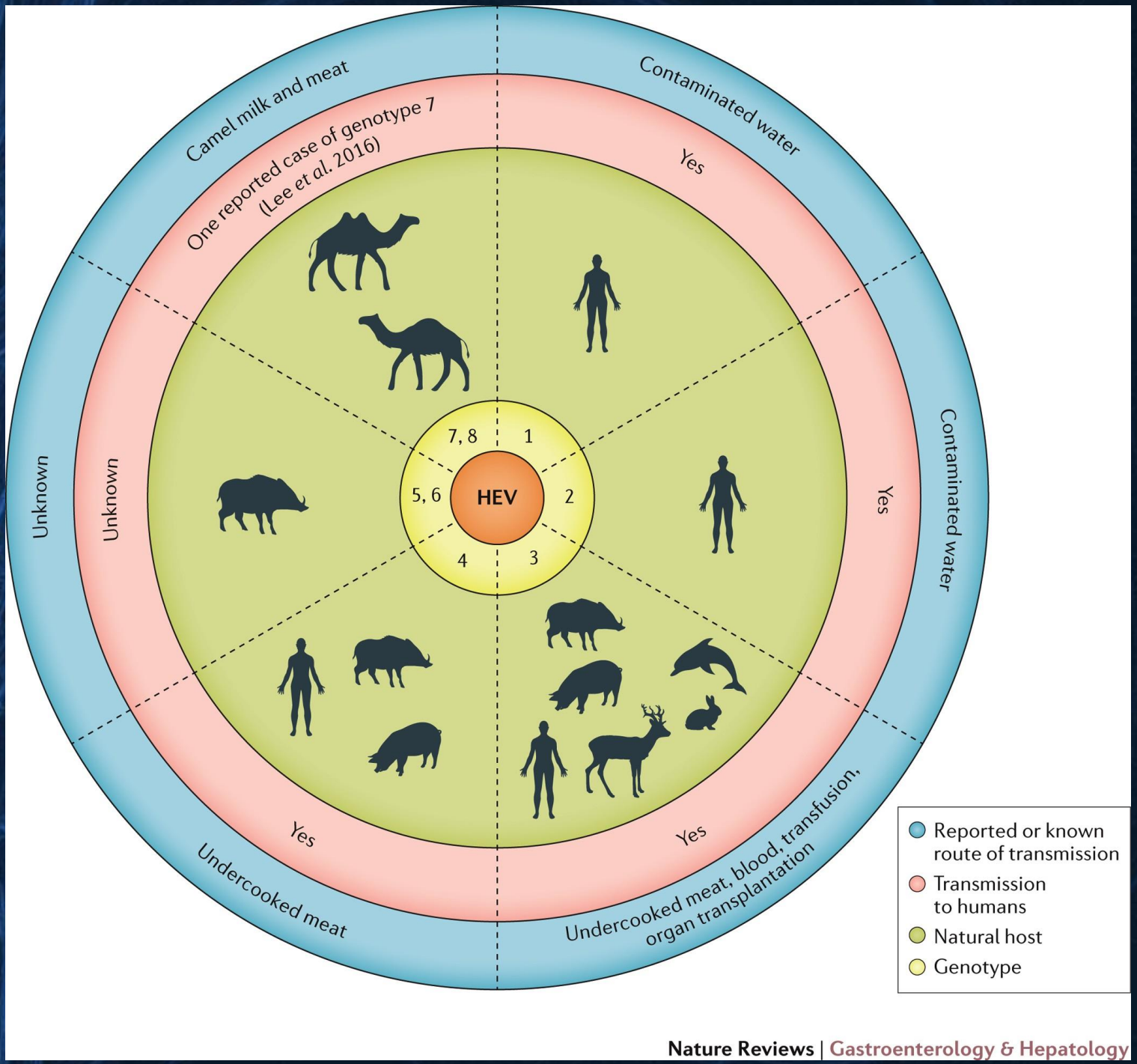
- HEV is a highly diverse pathogen that is witnessing a constant discovery of different variants across different animals the world over.
- Initially classified as a member of the Caliciviridae (certain biophysical and morphological similarities)
- Removed from the Caliciviridae family and became unclassified
- In 2004 the ICTV, re-classified HEV as a solitary virus in the Hepevirus genus and a member of the Hepeviridae family
- Hepeviridae family into two genera: Orthohepevirus and Piscihepevirus based on the analysis of the existing sequence information


Family: Hepeviridae
Genus: Orthohepevirus
A
Genotype: HEV 1 - 8
B
Genotype: Avian HEV
C
Genotype C1 - Rat HEV & C2 - Ferret HEV
D
Genotype: Bat HEV
Genus: Piscihepevirus
A
Genotype: cutthroat trout HEV


Worldwide
More distant
Avian
Bat
Rat
Ferret
Fish
gt 3
Mostly Asia, Africa
gt 1
gt 2
Africa and Mexico
Rabbit
Camel
Non
assigned
gt 4
China and
Southeast Asia
Swedish
moose
0.06

S/N	Genotype	Host	Region of Occurrence	Human Epidemic Disease	Human Sporadic Disease
1	1 (I)	Human (only)	West Africa, North Africa & Asia	Yes	Yes
2	2 (II)	Human (only)	Asia, Africa & Mexico	Yes	Yes
3	3 (III)	Human, Swine, & several other animals	North America, South America, Europe, Asia, & Africa	No	Yes
4	4 (IV)	Human, Swine, & several other animals	Americas, Europe & Asia	No	Yes
5	5 (V)	Wild Boar (only)	Asia (Japan)	No	No
6	6 (VI)	Wild Boar (only)	Asia (Japan)	No	No
7	7 (VII)	Human & Camel	North Africa & Middle East	No	Yes
8	8 (VIII)	Human & Camel	North Africa & Middle East	No	Yes



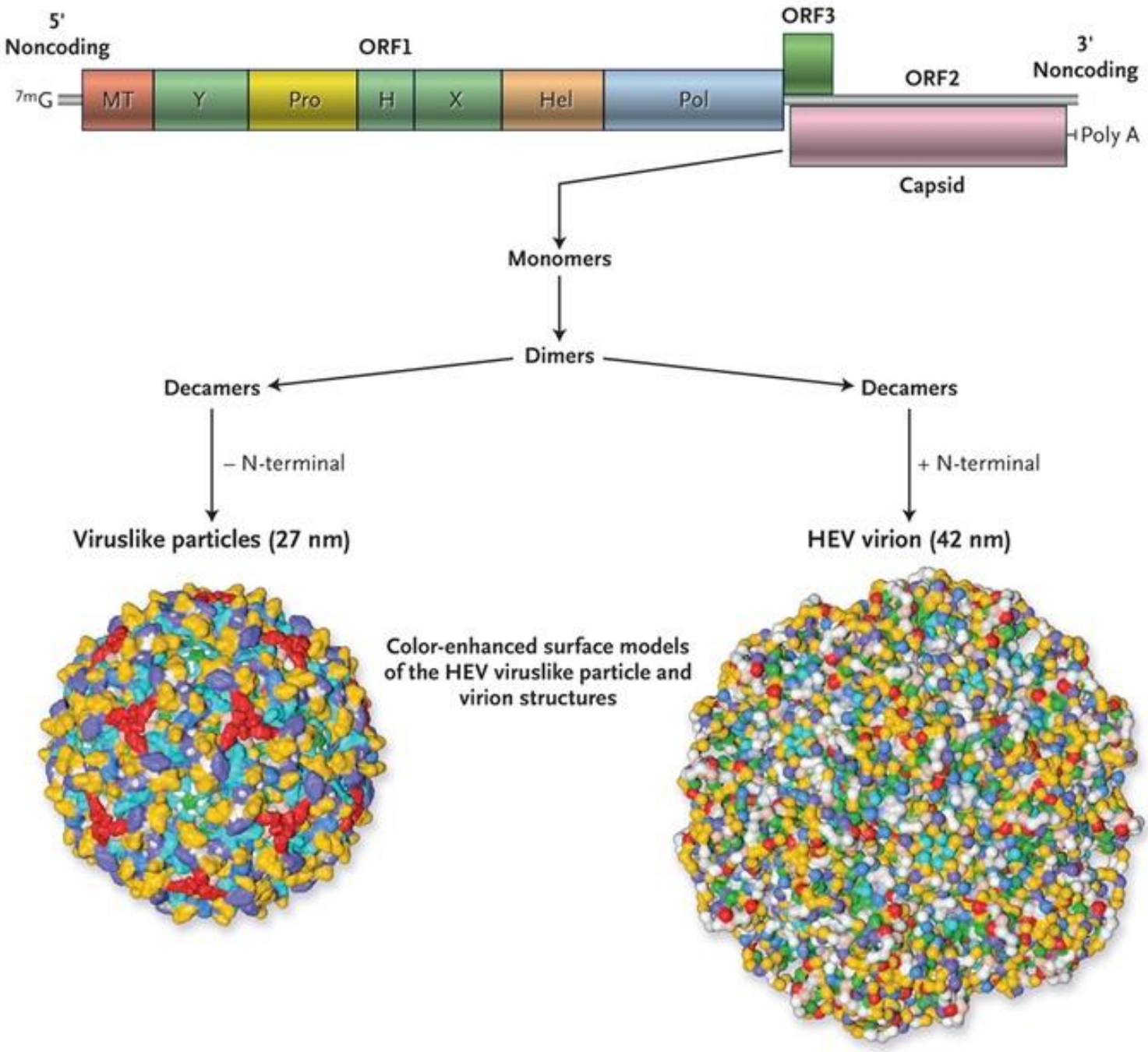

Camel milk and meat
One reported case of genotype 7 (Lee et al. 2016)
Contaminated water
Yes
Unknown
Unknown
Yes
Contaminated water
7, 8
1
5, 6
HEV
2
4
3
Yes
Undercooked meat
Yes
Undercooked meat, blood, transfusion, organ transplantation
Reported or known route of transmission
Transmission to humans
Natural host
Genotype
Nature Reviews | Gastroenterology & Hepatology

Molecular virology

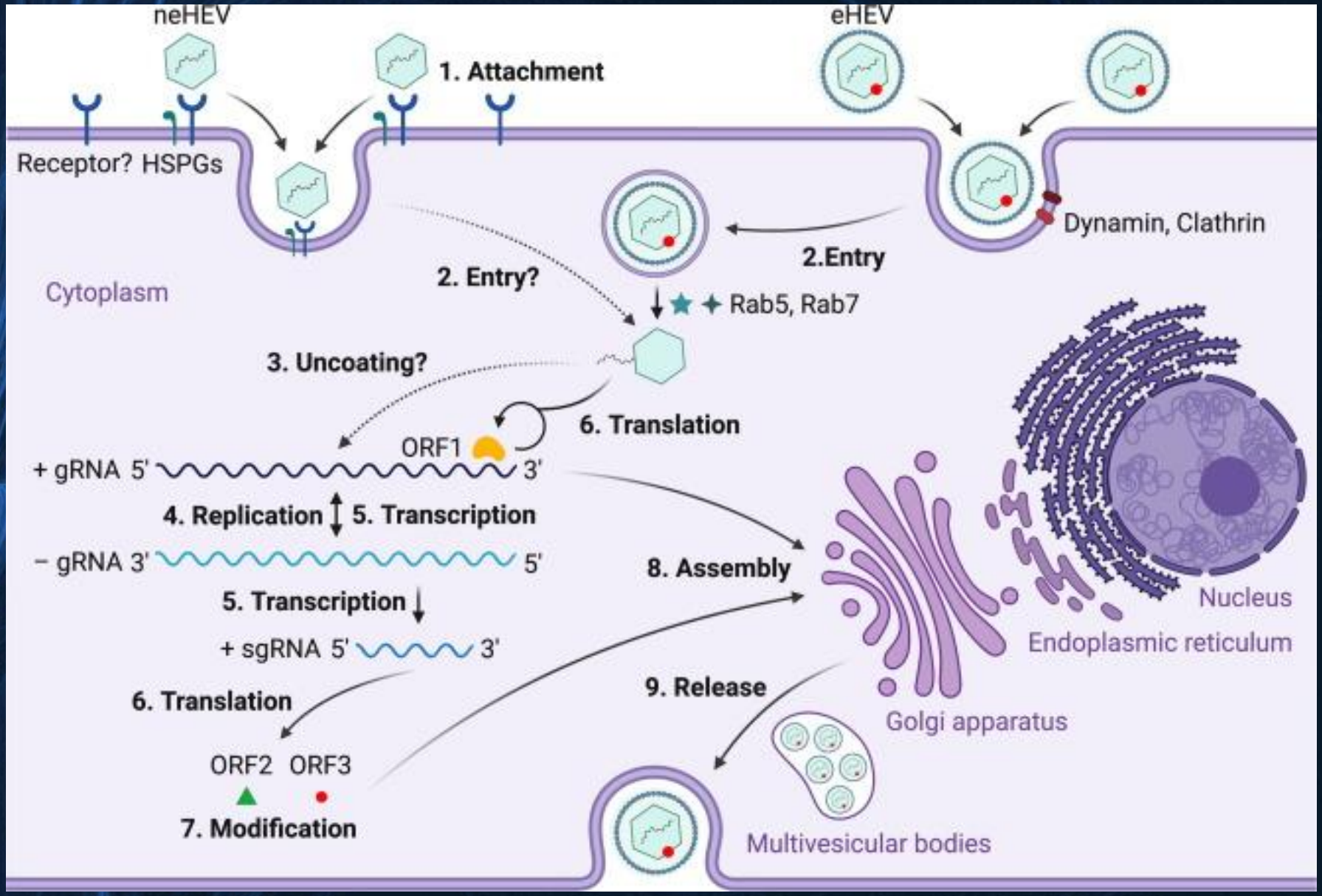
- A small non-enveloped virus with an approximate diameter of 27 – 34 nm.

- HEV is a single-stranded positive-sense RNA virus. The viral genome is capped (methylguanine) at the 5’ end and polyadenylated at the 3’ end. The virus is icosahedral in shape with a genome of 7.2 Kb in length

- The virus has three open reading frames (ORF) and three untranslated regions (UTR)



Color-enhanced surface models of the HEV viruslike particle and virion structures


neHEV
eHEV
1. Attachment
Receptor? HSPGs
Dynamin, Clathrin
2.Entry
2. Entry?
Cytoplasm
Rab5, Rab7
3. Uncoating?
6. Translation
ORF1
+ gRNA 5'
3'
4. Replication
5. Transcription
− gRNA 3'
5'
5. Transcription
+ sgRNA 5'
3'
8. Assembly
Nucleus
Endoplasmic reticulum
6. Translation
9. Release
Golgi apparatus
ORF2
ORF3
7. Modification
Multivesicular bodies

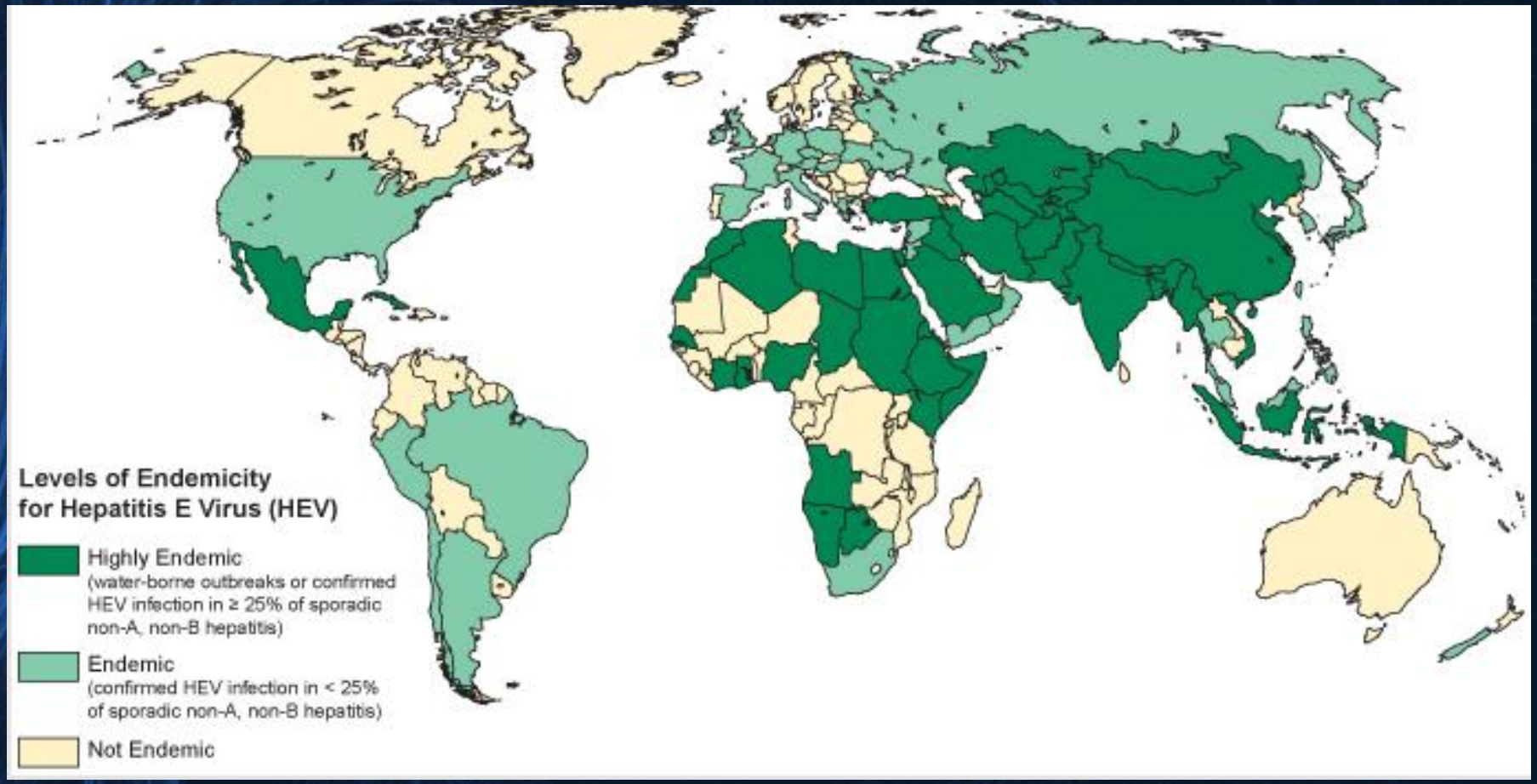
Epidemiology

- Global distribution with two separate

- Epidemiological patterns of distribution

- endemic disease regions: HEV1&2
- contaminated drinking water and poor sanitary hygiene

- sporadic disease: HEV3&4
- imported from travel to the endemic regions


Levels of Endemicity
for Hepatitis E Virus (HEV)
Highly Endemic
(water-borne outbreaks or confirmed HEV infection in ≥ 25% of sporadic non-A, non-B hepatitis)
Endemic
(confirmed HEV infection in < 25% of sporadic non-A, non-B hepatitis)
Not Endemic

Region Africa	Countries	Period	Number of Outbreaks	Number of Cases	References
	Algeria	1978–1987	2	> 300	(Coursaget, 1993; Grandadam, 2004)
	Central African Republic	2002–2005	2	> 1000	(Escribà, 2008; Goumba et al., 2011)
	Chad	1983–2004	2	> 1500	(van Cuyck-Gandré, 1997; World Health Organization, 2004)
	Djibouti	1992–1993	1	> 40	(Coursaget, 1998)
	Eritrea	I988 – 1989	1	> 750	(Tsega, 1991)
	Kenya	1991–2012	2	> 2,000	(Mast, 1994)
	Morocco	1994	1	> 75	(Benjelloun, 1997)
	Namibia	1983	1	> 200	(Isaäcson, 2000)
	Somalia	1988–1989	1	greater than11,000	(Bile, 1994; Mushahwar, 1993)
	South Sudan	2004–2013	2	> 7,700	(Pinoges, 2006; Thomson, 2013)
	Sudan	1984–2004	2	> 2,500	(McCarthy, 1994)
	Uganda	2007–2009	1	10,196	(Teshale, 2010)
Asia					
	Bangladesh	2008–2010	2	> 4,000	(Gurley, 2014; Harun-Or-Rashid, 2013)
	Burma (Myanmar)	1976–1989	3	20,510	(Gideon Informatics et al., 2020)
	China	1982–1988	9	> 119,280	(Zhuang, 1991)
	India	1955–1991	5	> 135,500	(Khuroo, 1980; Viswanathan, 1957; Naik, 1992; Jameel, 1992; Sreenivasan, 1978)
	Indonesia	1987–2004	4	greater than5,000	(World Health Organization, 2005; Sedyaningsih-Mamahit, 2002; Corwin, 1995)
	Nepal	1973–2006	4	> 14,000	(Labrique, 1999; Kane, 1984)
	Pakistan	1984–1994	6	> 4,000	(Labrique, 1999)
	Vietnam	1994	1	–	(Corwin, 1996)
Central America					
	Mexico	1986–1987	2	> 200	(Velazquez, 1990)

HEV infected person
TRANSPLANT RECIPIENT
Person-to-person transmission
HEV contaminated food and drink
Faecal-oral transmission usually by HEV – 1 and HEV -2
Transfusion transmission
HEV infected persons
Faecal contamination of water source by infected persons
HEV contaminated water
Sewage from HEV infected animals
Vertical transmission
Animal-to-human direct contact transmission
Zoonotic transmission usually by HEV – 3 and HEV - 4
Animal product from HEV infected animals consumed by an immunocompromised individual
Contaminated animal products
HEV infected animals

Sero-epidemiology

- Industrialised nations have lower (1%-52%) HEV seroprevalence when compared to the developing regions (4%-94%).
- Most of the seroprevalence studies were conducted among different groups including, the healthy general population, healthy blood donors, population with HIV, and those exposed to animals.
- Faber and colleagues conducted a study on the seroprevalence of HEV among adults in Germany. The study showed anti-HEV IgG positivity of 16.8% in the adult population
- Spain conducted among the general population, the HEV seroprevalence rate was 1.6%

Transactions of the Royal Society of Tropical Medicine and Hygiene 106 (2012) 528–531

Contents lists available at SciVerse ScienceDirect

Transactions of the Royal Society of Tropical Medicine and Hygiene

journal homepage: http://www.elsevier.com/locate/trstmh

Seroepidemiology of hepatitis A and E virus infections in Tehran, Iran: a population based study

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Infection
DOI 10.1007/s15010-015-0807-5

REVIEW

Hepatitis E virus in the countries of the Middle East and North Africa region: an awareness of an infectious threat to blood safety

Soha Yazbek[1] ·

Category/population studied	Number of participants	Mean age (age group)	Anti-HEV IgG (%)	Anti-HEV IgM (%)	HEV-RNA (%)	Refere
Iran						
Hemodialysis						
Hemodialysis patients[c]	80	55.69 ± 14.70 (26–80)	6	–	–	[58]
Healthy individuals (control)	276	51.73 ± 15.10 (24–77)	3	–	–	
Kidney transplant patients[c]	–	–	30	–	–	[59]
Hemodialysis patients[c]	324	53.5 ± 15.1	7	–	–	[60]
Others						
Pregnant women	136	(14–39)	4	–	–	[61]
General population of Mashhad, northeast of Iran	1582	29.06 ± 18.513 (<5 to ≥65)	14	–	–	[62]
HIV-infected patients	100	(34–43)	10	0	0	[63]
Population based (Tehran)	551	41.28 ± 16.96 (1–83)	9	–	–	[64]
Active health centers in Khorramabad (Western Iran)	400	36 (>20)	8	–	–	[65]
Community based (Sari district)	1080	(2–25)	2	–	–	[66]
Population based (Isfahan Province)	816	(6 to ≥50)	4	–		[67]
Population based (Nahavand)	1824	34.7 ± 19.5 (6 to >70)	9	–	–	[68]
Iraq						
Outbreak						
Al-Sadr city, Baghdad	270	–	21	–	–	[69]
Al-Sadr city, Baghdad	268	(<10 to >40)	–	38	–	[70]
Hepatitis						
Patients with suspected acute viral hepatitis	2692	(<5 to >45)	–	2	–	[71]
Others						
Thai Troops Deployed with U.N. Peacekeeping Forces in Iraq	869	(21–55)	21	2	–	[72]
Refugee Kurds from Iraq	637	24 ± 8.4 (0.5–55)	18	–	–	[73]
Israel						
Others						
Travelers returning from tropical countries	4,970	37 ± 14.2	0.38	–	–	[74]
Backpackers to Tropical Countries	105	22.3 ± 2.5 (<32)	0	–	–	[75]
Saudi Arabia						
Hepatitis						
Patients with acute viral hepatitis	246	(<10 to >21)	–	13	–	[76]
Hemodialysis						
Hemodialysis patients[c]	83	39.0 ± 17.8 (7-82)	7	5	–	[77]
Healthy controls	400	40.3 ± 18.5 (10-78)	11	0.30	–	

Microbial Pathogenesis
Volume 110, September 2017, Pages 252-256

Hepatitis E virus seroprevalence rate among Eastern Mediterranean and middle eastern countries; A systematic review and pooled analysis

Mohammad Hadi Karbalaie Niya [a, b, c], Mohammad Saeid Rezaee-Zavareh [a, b, d], Alireza Ranaei [a, b, d], Seyed Moayed Alavian [a, b]

Table 2. Hepatitis E Virus Prevalence and Number of People Living With This Infection in the WHO Eastern Mediterranean Region and Middle East [a]

Country Name	Prevalence by HEV IgG Ab		Country Population	Estimated IgG positive
	Studies N (patients)	IgG Positive N (%) (95% CI)		
Afghanistan	1 (540)	78 (14.44) (11.67-17.59)	32,530,000	4,697,332
Egypt	5 (1954)	395 (20.21) (18.47-22.03)	91,510,000	18,494,171
Iran	31 (16315)	1788 (10.95) (10.48-11.44)	79,110,000	8,662,545
Israel	2 (2145)	114 (5.31) (4.42-6.32)	8,463,000	449,385
Pakistan	1 (52)	28 (53.84) (40.39-66.88)	188,900,000	101,703,760
Saudi Arabia	4 (2312)	353 (15.26) (13.84-16.77)	31,540,000	4,813,004
Sudan	1 (80)	30 (37.50) (27.48-48.39)	40,230,000	15,086,250
Somalia	1 (145)	122 (84.13) (77.54-89.38)	10,790,000	9,077,627
Tunisia	5 (3903)	222 (5.68) (4.99-6.44)	11,110,000	631,048
Turkey	9 (3402)	501 (14.72) (13.56-15.94)	78,666,000	11,579,635
United Arab Emirates	1 (469)	93 (19.82) (16.41-23.61)	9,157,000	1,814,917
Yemen	1 (356)	38 (10.67) (7.78-14.19)	26,832,000	2,862,974
Middle East	51 (26953)	3282 (12.17) (11.79-12.57)	325,278,000	39,586,333
EMRO	53 (26626)	3147 (11.81) (11.43-12.21)	521,709,000	61,613,833
Total	62 (31673)	3762 (11.87) (11.52-12.23)	608,838,000	72,269,071

Pathogenesis

- The pathogenesis of hepatitis E is poorly understood and is largely based on the data from a few human cell culture systems and animal models
- The incubation period after viral entry into the host usually through the gastrointestinal tract is 14 days to about 10 weeks
- Viraemia, which often coincides with faecal HEV excretion appears few days before the onset of clinical symptoms and persists for 14 – 21 days thereafter
- Viral faecal excretion may persist for about 16 weeks (as shown in experimental animals) with a longer detection window than viremia

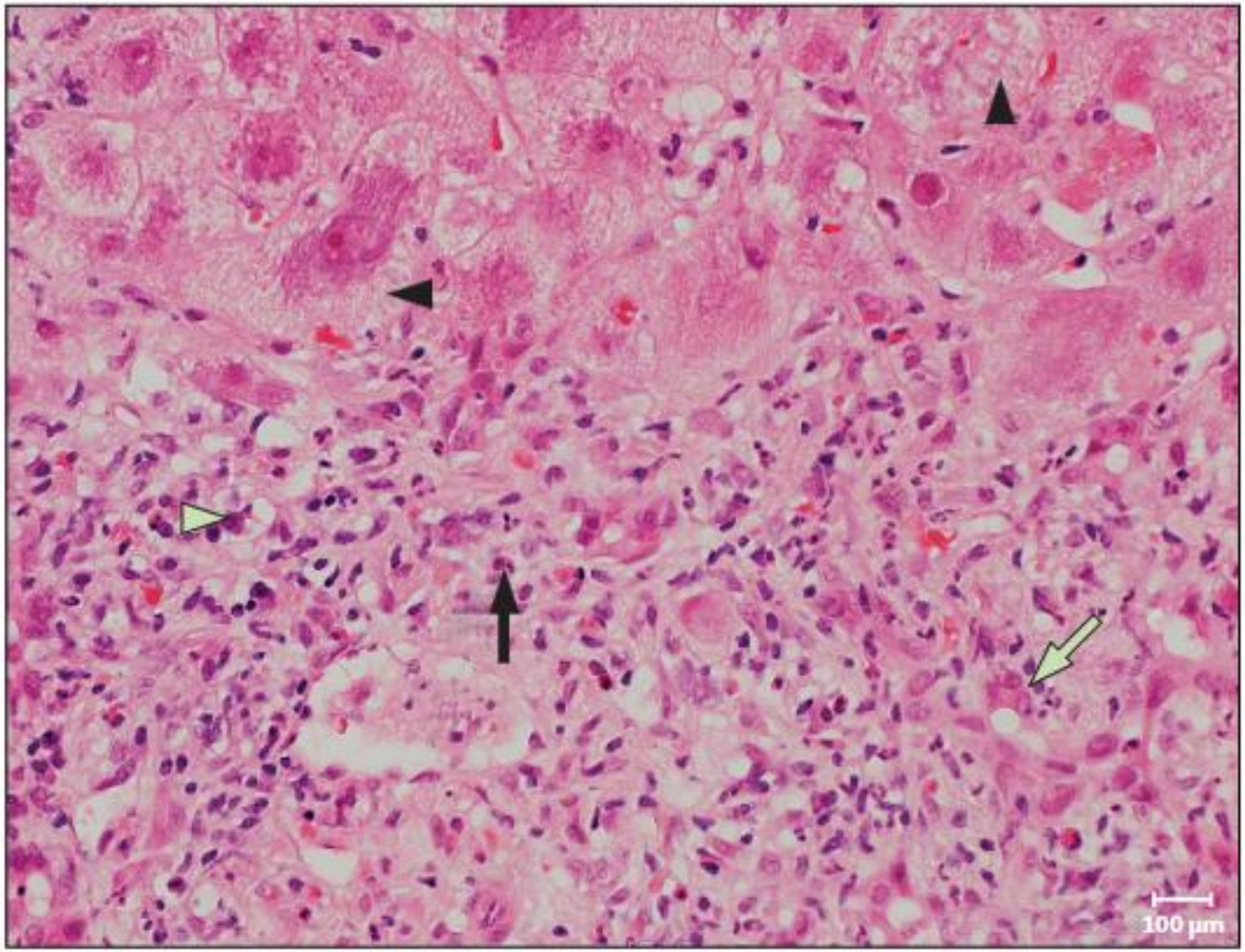


***Figure* 3: Liver histology of patient with acute autochthonous hepatitis E**

Section shows expansion of portal tracts by an intense portal mixed inflammatory infiltrate with occasional lymphoid aggregates and bile ductular proliferation (pale green arrow; haematoxylin and eosin stain). The inflammatory infiltrate is made up of lymphocytes, including plasma cells (pale green arrow head) and polymorphs, including eosinophils (black arrow). Periportal hepatocytes show some ballooning degeneration (black arrow head).

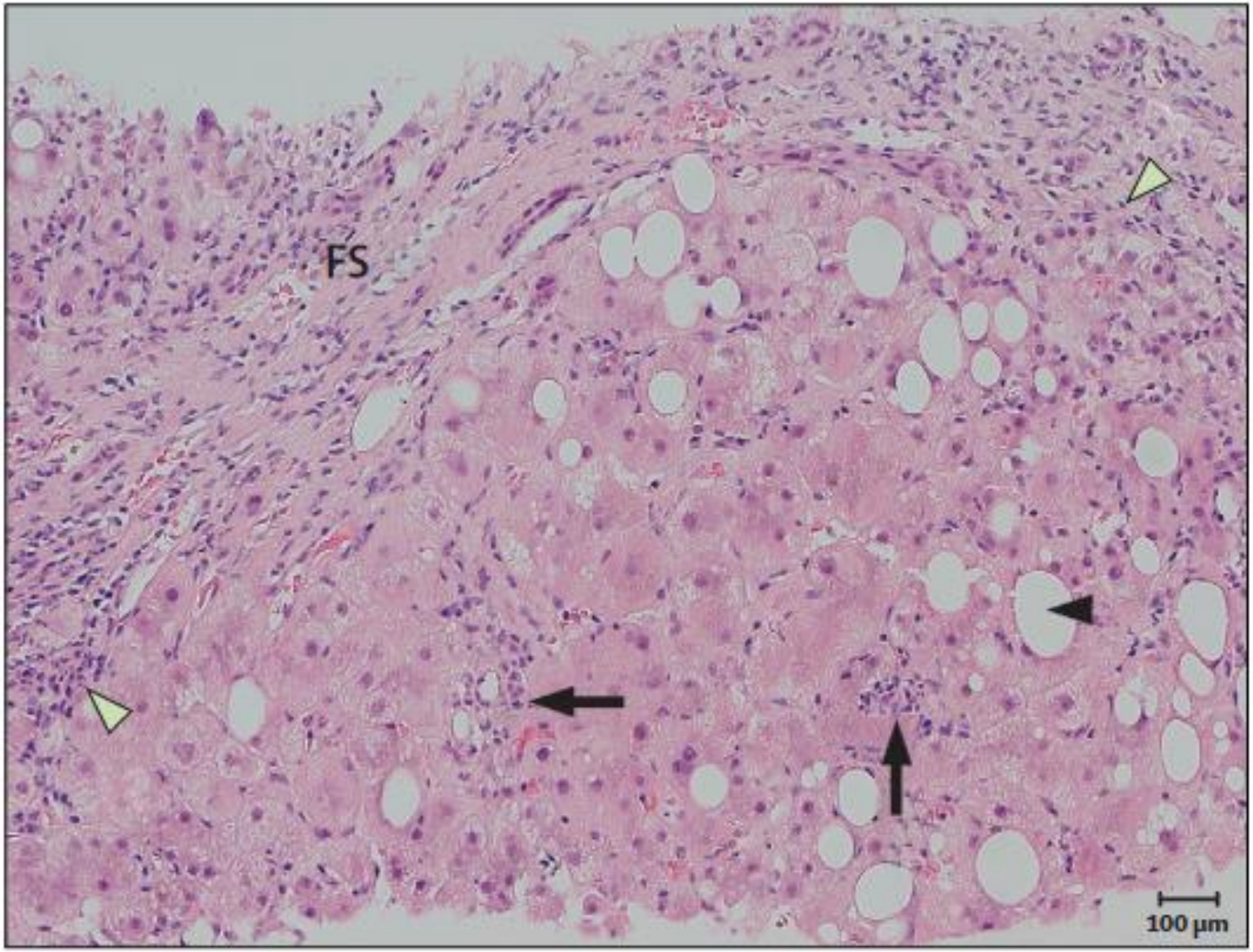
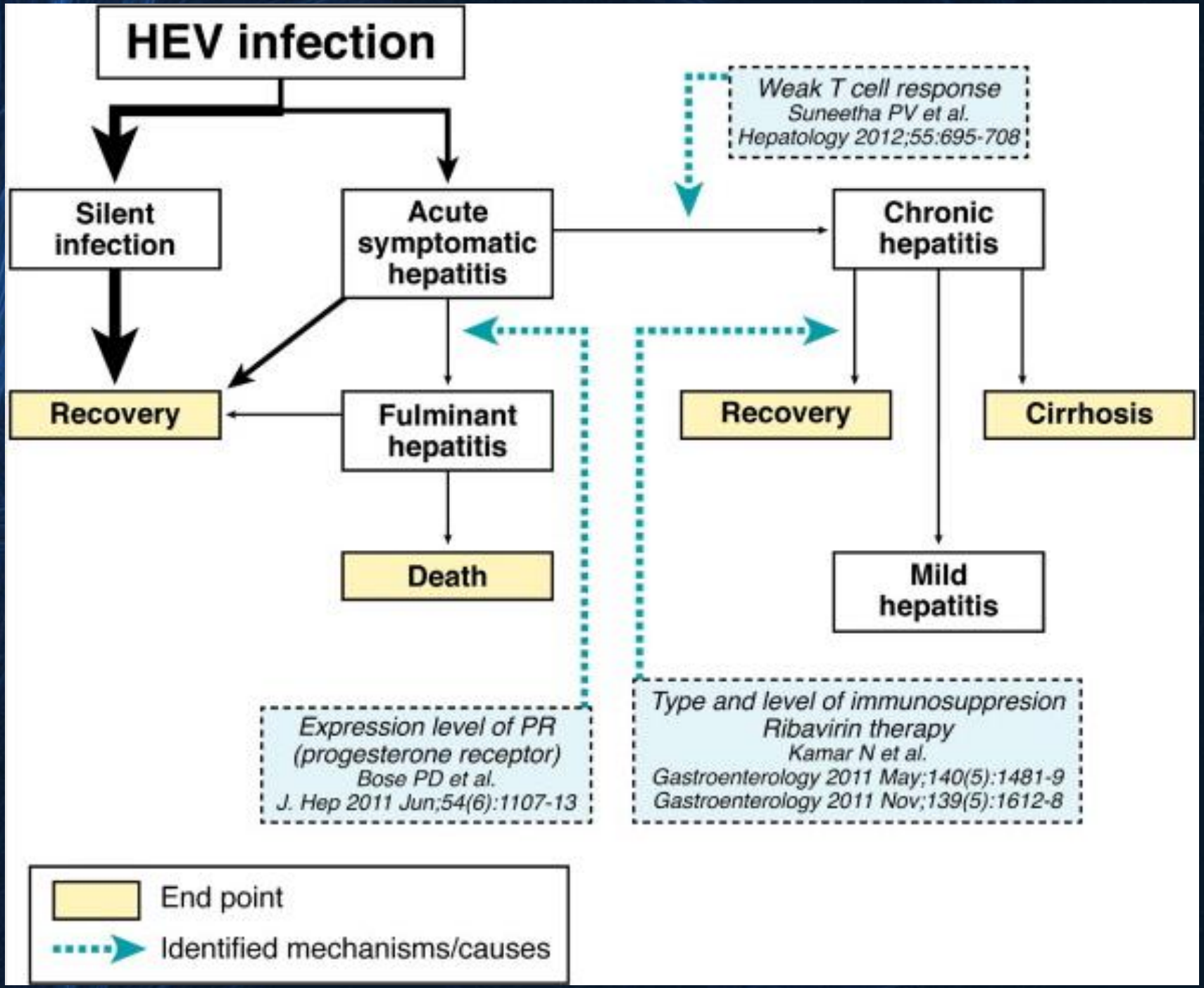
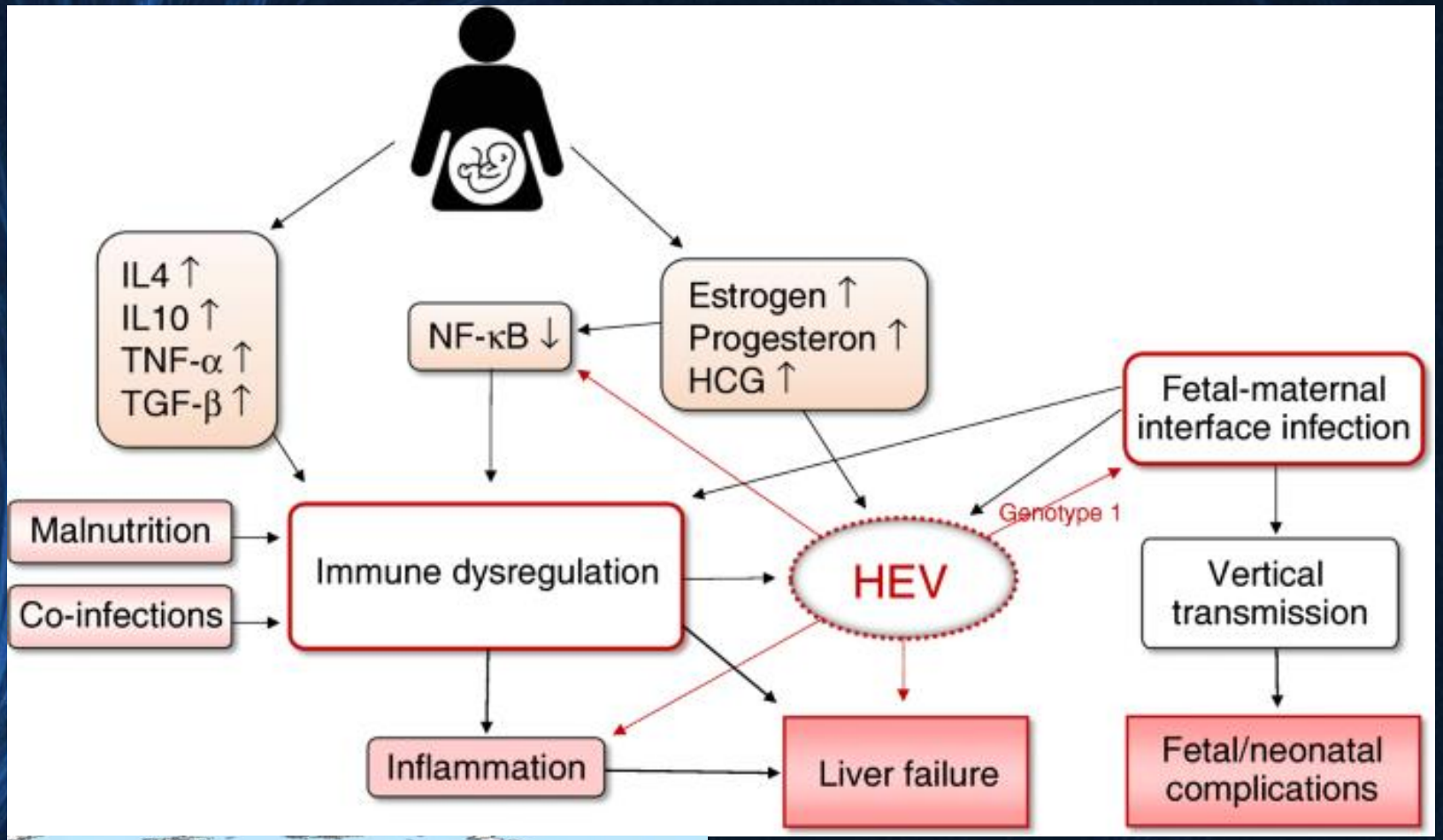
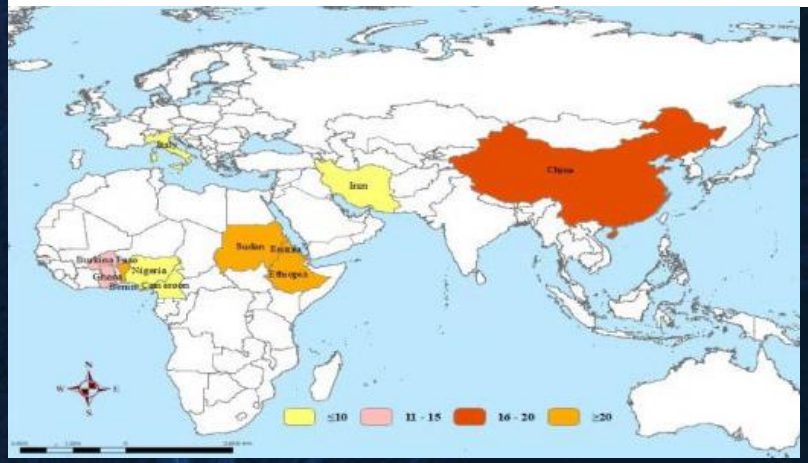


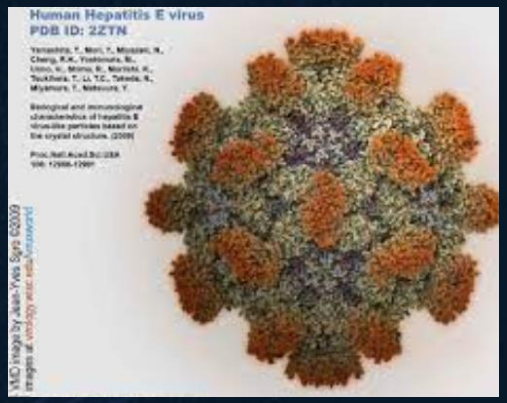
***Figure 4*: Liver biopsy in a patient with hepatitis E and ethanolic cirrhosis**

Section shows fibrosis, nodule formation, and mixed inflammatory infiltration (lymphoplasmocytic, eosinophils, and neutrophils) along fibrous septae (FS) with extension into the parenchyma suggesting interface hepatitis (pale green arrow heads). Bile duct proliferation is seen with intrahepatic and intracanalicular bile stasis. The hepatocytes in the nodules show macrovascular fatty change (black arrow head) along with inflammatory cells and focal hepatocytic necrosis (black arrows). These features were consistent with an acute insult to an underlying cirrhotic process.


HEV infection
Silent infection
Acute symptomatic hepatitis
Chronic hepatitis
Weak T cell response
Suneetha PV et al.
Hepatology 2012;55:695-708
Recovery
Fulminant hepatitis
Recovery
Cirrhosis
Death
Mild hepatitis
Expression level of PR (progesterone receptor)
Bose PD et al.
J. Hep 2011 Jun;54(6):1107-13
Type and level of immunosuppresion
Ribavirin therapy
Kamar N et al.
Gastroenterology 2011 May;140(5):1481-9
Gastroenterology 2011 Nov;139(5):1612-8
End point
Identified mechanisms/causes


IL4 ↑
IL10 ↑
TNF-α ↑
TGF-β ↑
NF-κB ↓
Estrogen ↑
Progesteron ↑
HCG ↑
Fetal-maternal interface infection
Malnutrition
Co-infections
Immune dysregulation
HEV
Genotype 1
Vertical transmission
Inflammation
Liver failure
Fetal/neonatal complications


China
Iran
Sudan
Nigeria
Ethiopia
≤10
11 - 15
16 - 20
≥20

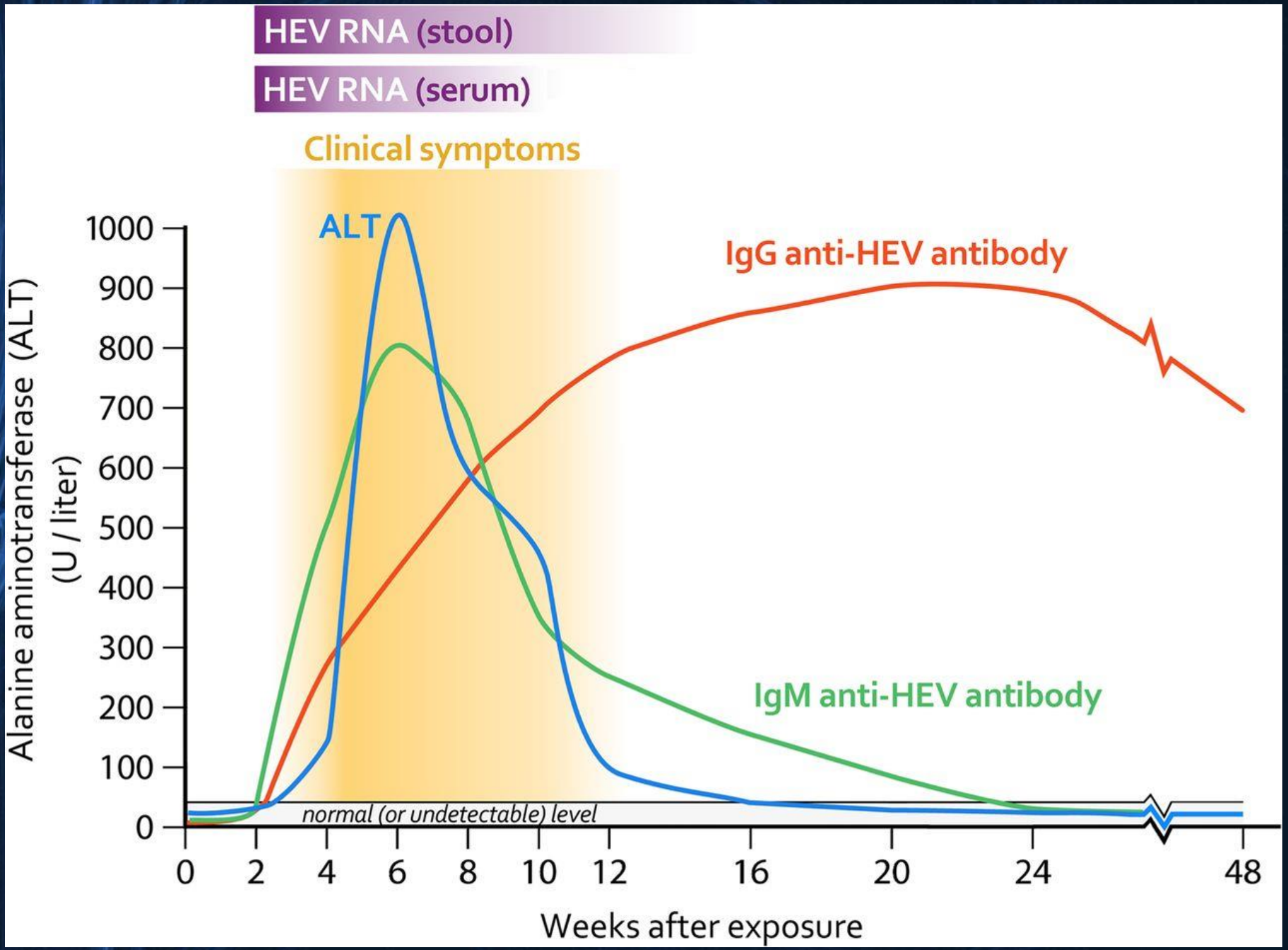

Human Hepatitis E virus
PDB ID: 2ZTN

Clinical features of hepatitis E

Most HEV infections have clinically silent course

• Incubation period	3 – 8 weeks
• Prodromal phase	Short
• Symptoms or jaundice	Days to several weeks
• Most cases are self-limited	
• Case fatality rate	**0 – 10 %** **20 % in pregnant women**

Hoofnagle JH et al. N Engl J Med 2012 ; 367 : 1237 – 44 .

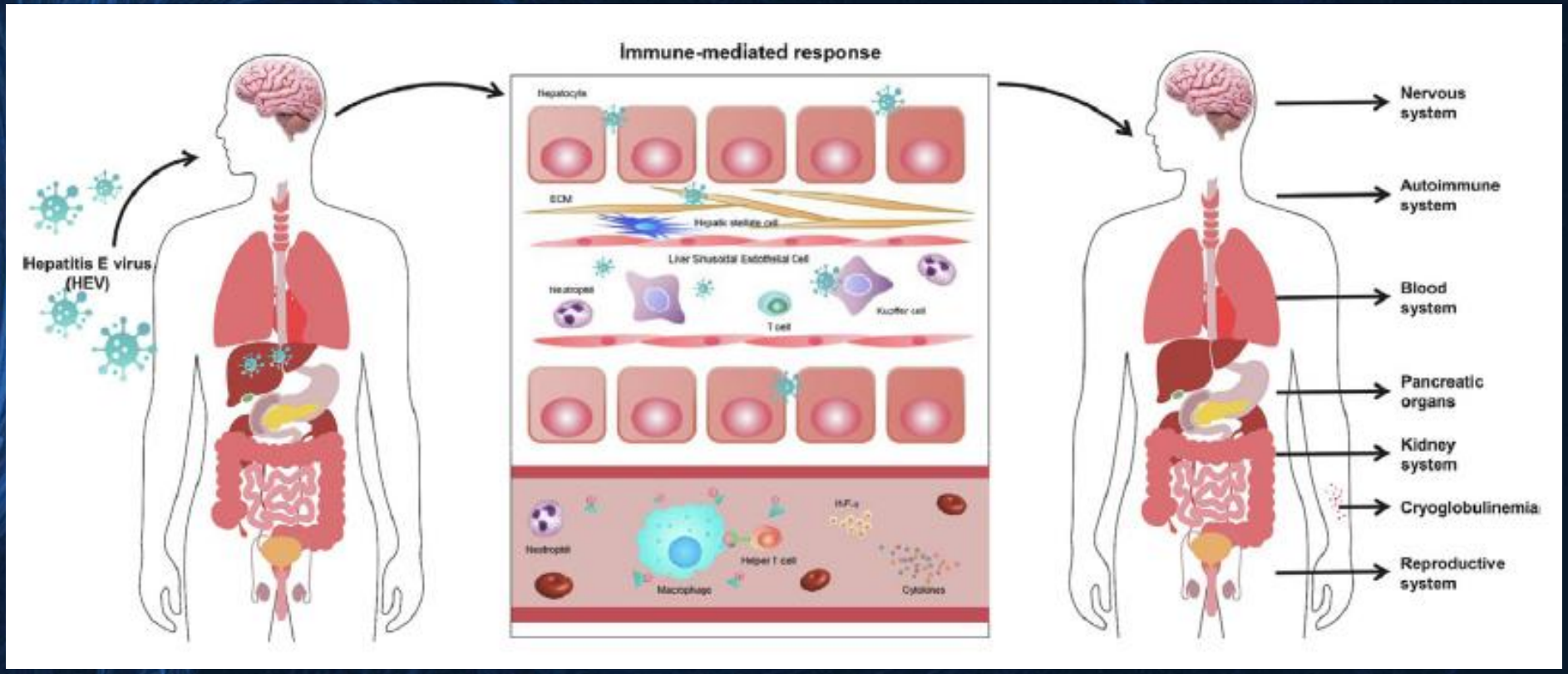

HEV RNA (stool)
HEV RNA (serum)
Clinical symptoms
ALT
IgG anti-HEV antibody
IgM anti-HEV antibody
normal (or undetectable) level
Alanine aminotransferase (ALT)
(U / liter)
1000
900
800
700
600
500
400
300
200
100
0
0
2
4
6
8
10
12
16
20
24
48
Weeks after exposure

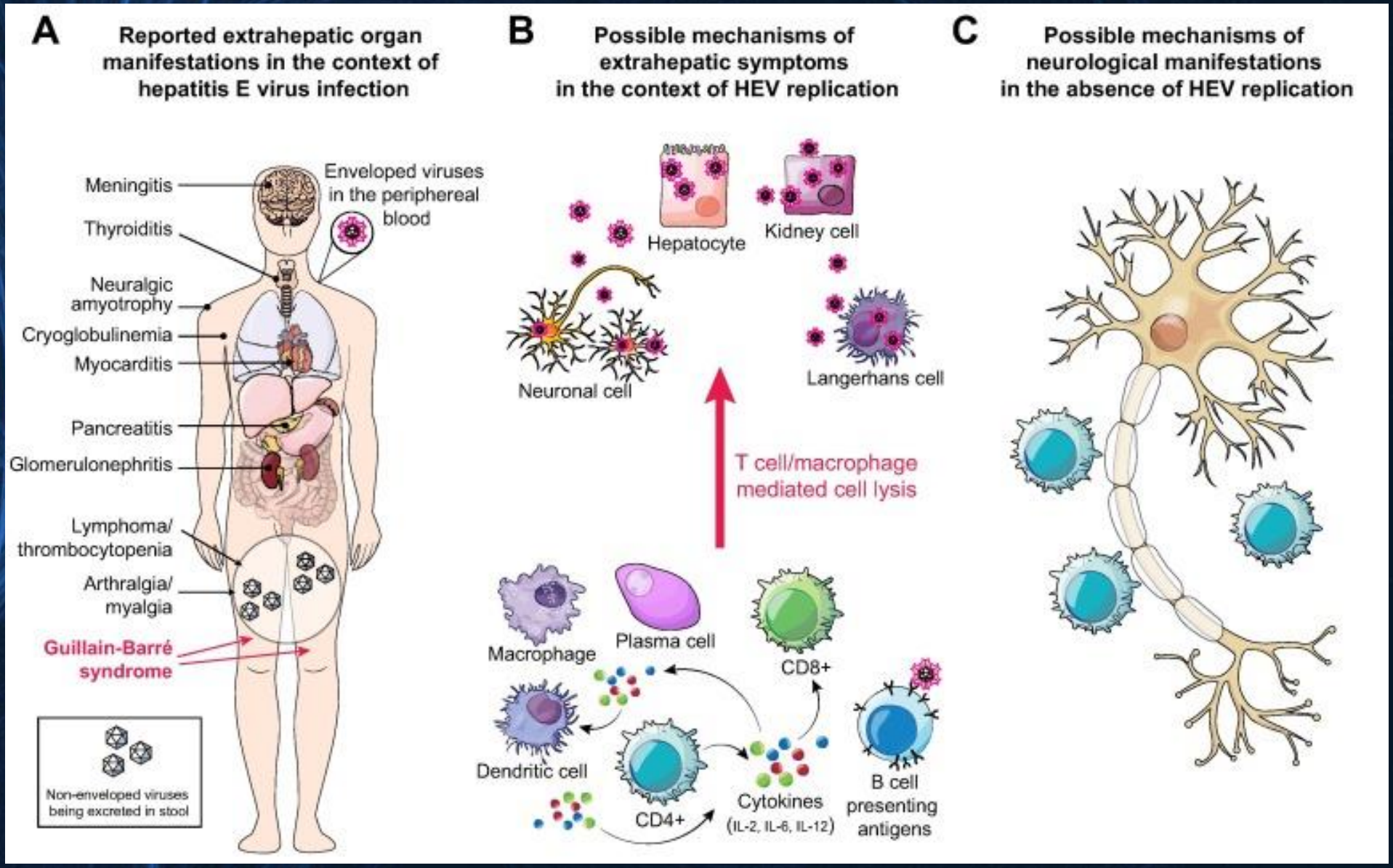
Clinical presentation of Acute icteric hepatitis.

S/N	Phases	Duration	Symptoms / Signs	Laboratory Markers
1	Prodromal	1 – 10 days	Low grade fever, Anorexia, Nausea (intense), Vomiting, Myalgia, Malaise	↑ ALT, AST, Serum bilirubin (Normal or Elevated)
2	Icteric	14 – 28 days (may continue for weeks and months leading to cholestasis)	Jaundice, Improved appetite, Declining prodrome symptoms, Tender hepatomegaly ± splenomegalyCholestatic symptoms; clay stool, dark urine, deep jaundice, intense pruritus, poor sleep, impaired work performance, poor quality of life	↓ ALT, AST, Serum bilirubin ↑
3	Convalescence		*Recovery and disappearance of symptoms	Returns to Normal

*Recovery usually spontaneous and complete. If recovery does not occur, it may progress to acute liver failure. ALT, alanine aminotransferase; AST, aspartate aminotransferase; ↑, increase; ↓, decrease.

Characteristic	Value	
	HAV	HEV
Incubation period (median no. of days)	30	40
Dose-dependent severity	No	Yes
Mortality (%)	0.1–2.1	0.2–4
Mortality in pregnancy	No difference	Up to 25%
Chronic disease	No	Yes (HEV3, HEV4)
Developed countries	Epidemic, endemic	Sporadic, travel associated (HEV1, HEV2) Sporadic, endemic (HEV3, HEV4)
Developing countries	High seropositivity, rare clinical disease	Epidemic, endemic
Age group	Adolescents, young adults	Adolescents, young adults (HEV1, HEV2) Older adults (HEV3, HEV4)
Sex	No difference	Males more commonly affected


Hepatitis E virus
(HEV)
Immune-mediated response
Hepatocyte
ECM
Hepatic stellate cell
Liver Sinusoidal Endothelial Cell
Neutrophil
T cell
Kupffer cell
Neutrophil
Macrophage
Helper T cell
Cytokines
Nervous system
Autoimmune system
Blood system
Pancreatic organs
Kidney system
Cryoglobulinemia
Reproductive system

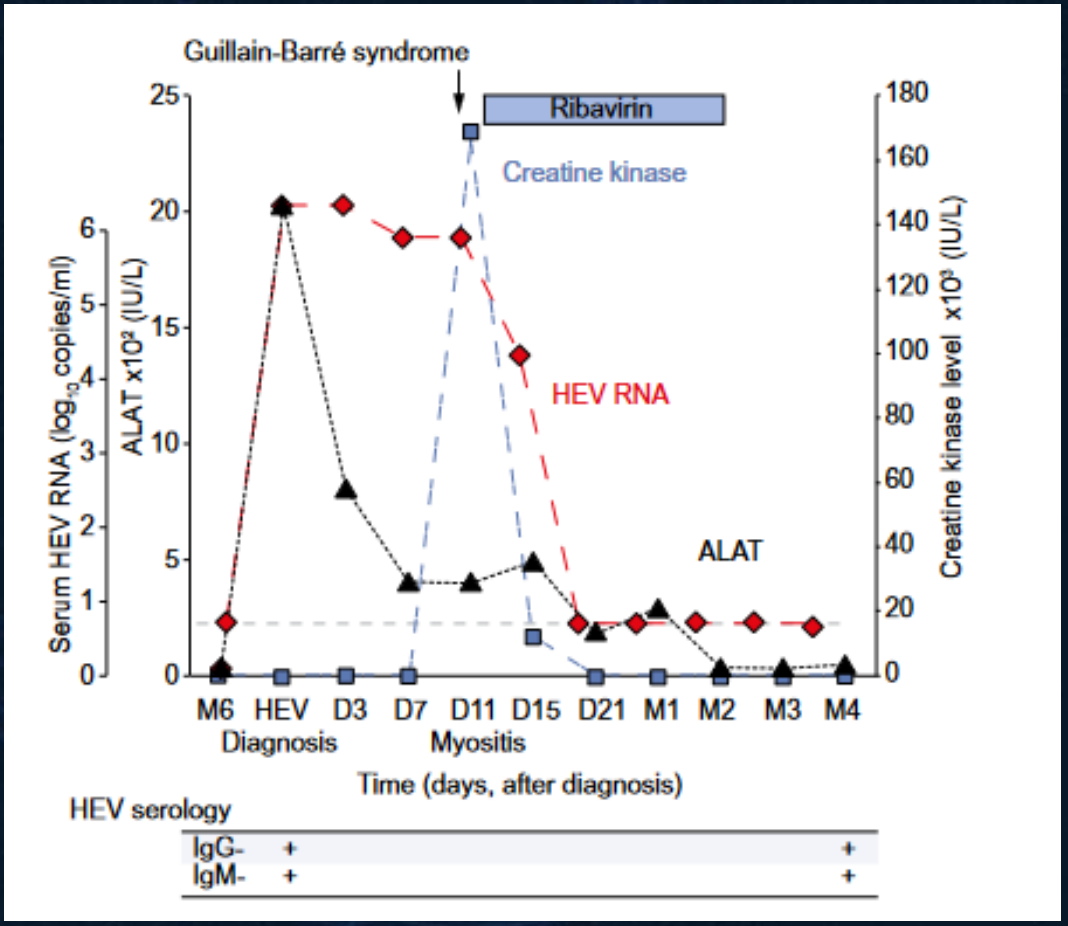

A
Reported extrahepatic organ manifestations in the context of hepatitis E virus infection
Meningitis
Thyroiditis
Neuralgic amyotrophy
Cryoglobulinemia
Myocarditis
Pancreatitis
Glomerulonephritis
Lymphoma/ thrombocytopenia
Arthralgia/ myalgia
Guillain-Barré syndrome
Enveloped viruses in the peripheral blood
Non-enveloped viruses being excreted in stool
B
Possible mechanisms of extrahepatic symptoms in the context of HEV replication
Hepatocyte
Kidney cell
Neuronal cell
Langerhans cell
T cell/macrophage mediated cell lysis
Macrophage
Plasma cell
CD8+
Dendritic cell
CD4+
Cytokines (IL-2, IL-6, IL-12)
B cell presenting antigens
C
Possible mechanisms of neurological manifestations in the absence of HEV replication

EASL EUROPEAN ASSOCIATION FOR THE STUDY OF THE LIVER | JOURNAL OF HEPATOLOGY

Hepatitis E virus-induced severe myositis

To the Editor:

Genotype 3 hepatitis E virus (HEV3) infection is responsible for self-limiting acute hepatitis, chronic HEV3 infection leading to cirrhosis in immunosuppressed patients, and several extra-hepatic manifestations, i.e., neurological symptoms, kidney injury, and severe thrombocytopenia [1–5]. Ribavirin therapy has been shown to be an efficient therapy for chronic HEV infection [6,7]. Herein, we report on a first case of Guillain–Barré syndrome merular filtration rate (40 ml/min)]. Rapidly after the initiation of both therapies, CK and ALT levels decreased and returned to within the normal range, respectively, 3 and 30 days later. Serum HEV RNA became undetectable by day 15, but ribavirin therapy was continued for 3 months as initially scheduled. Two months after ribavirin was stopped, serum HEV RNA was still negative. Fifteen days after HEV clearance, progressive recovery of mobility was noted.



frontiers in Microbiology

ORIGINAL RESEARCH
published: 08 October 2021
doi: 10.3389/fmicb.2021.737486

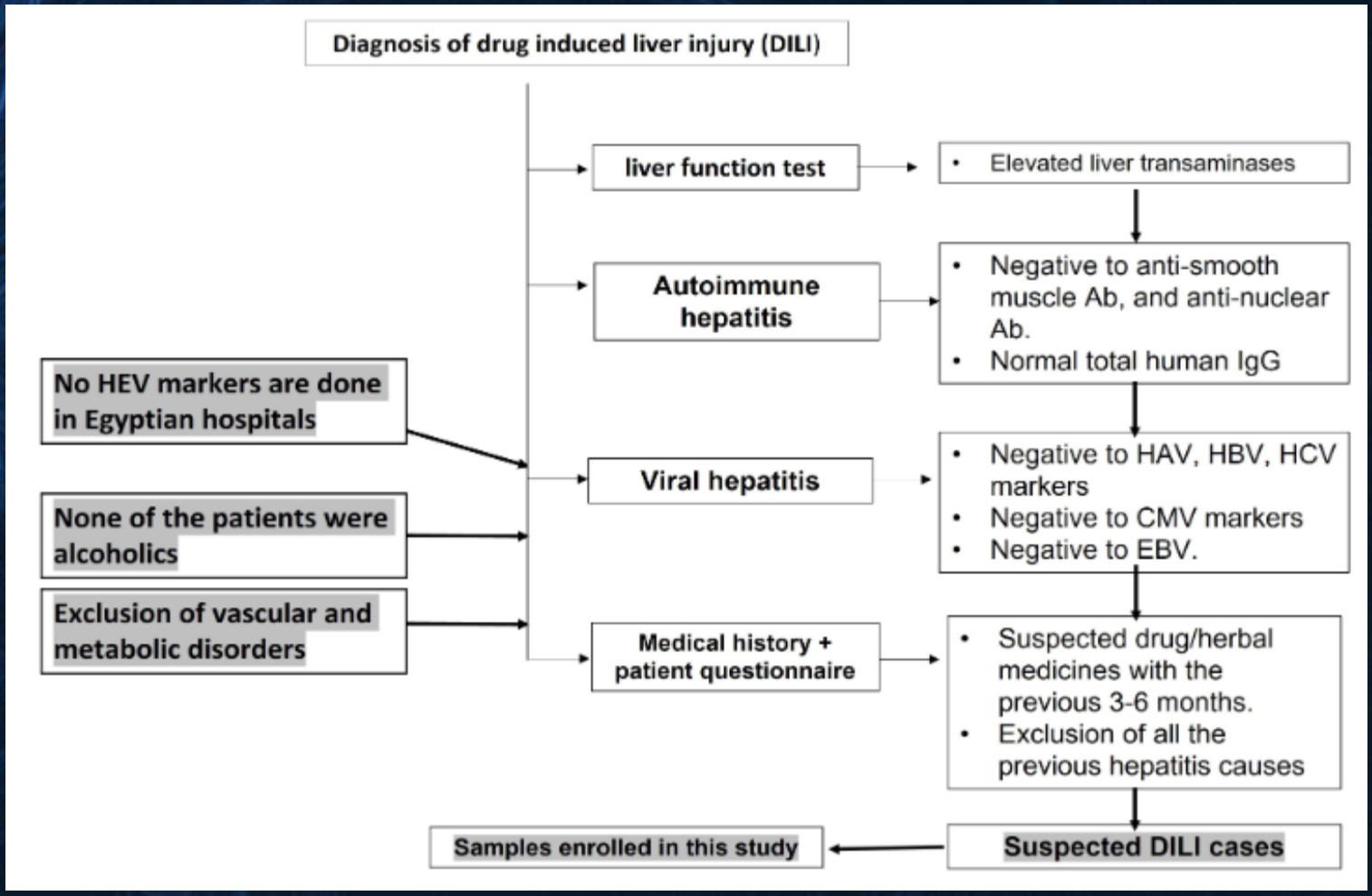
The Unmet Needs of Hepatitis E Virus Diagnosis in Suspected Drug-Induced Liver Injury in Limited Resource Setting

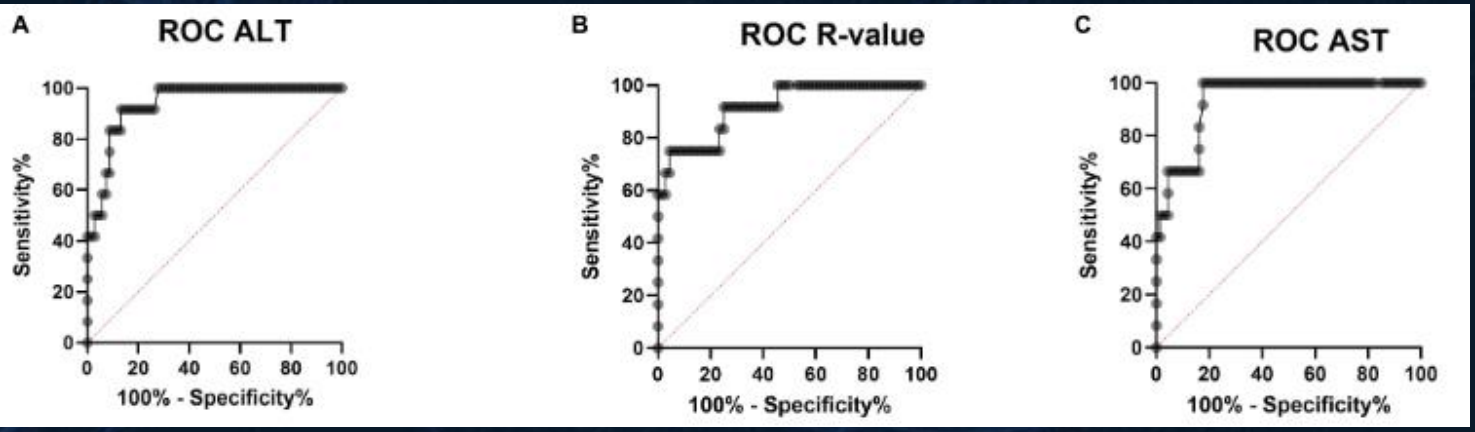
Mohamed A. El-Mokhtar[1,2], Haidi Karam-Allah Ramadan[3], Marwa M. Thabet[4], Alaa S. Abd-Elkader[4], Magdy Fouad[5], Mohammad M. Sallam[6], Elsayed A. Elgohary[6], Amer Ali Abd El-Hafeez[7,8], Mona Embarek Mohamed[1] and Ibrahim M. Sayed[1]**

[1] Department of Medical Microbiology and Immunology, Faculty of Medicine, Assiut University, Asyut, Egypt, [2] Microbiology and Immunology Department, Faculty of Pharmacy, Sphinx University, Asyut, Egypt, [3] Department of Tropical Medicine and Gastroenterology, Faculty of Medicine, Assiut University, Asyut, Egypt, [4] Department of Clinical pathology, Faculty

Results: Out of 80 samples, 12 samples were positive for anti-HEV IgM and anti-HEV IgG, and HEV RNA was detected in seven samples. The median viral load was 3.46×10^3 IU/ml, and the isolated viruses belonged to HEV genotype 1. The level of liver enzymes such as alanine transaminase (ALT) and aspartate transaminase (AST), but not alkaline phosphatase (ALP), was significantly higher in HEV confirmed cases than in non-HEV confirmed cases. We identified a plasma ALT level of at least 415.5 U/L and AST level of at least 332 U/L; ALT/ALP ratio of at least 5.08 could be used as a guide for the patients diagnosed as DILI to be tested for HEV infection. The previous liver function parameters showed high sensitivity and good specificity.

Conclusion: Hepatitis E virus was detected in suspected DILI cases. The diagnosis of DILI is not secure until HEV testing is done. Liver function parameters can be used as a guide for HEV testing in suspected DILI cases in countries with limited resources.


Diagnosis of drug induced liver injury (DILI)
liver function test
Elevated liver transaminases
Autoimmune hepatitis
Negative to anti-smooth muscle Ab, and anti-nuclear Ab.
Normal total human IgG
No HEV markers are done in Egyptian hospitals
Viral hepatitis
Negative to HAV, HBV, HCV markers
Negative to CMV markers
Negative to EBV.
None of the patients were alcoholics
Exclusion of vascular and metabolic disorders
Medical history + patient questionnaire
Suspected drug/herbal medicines with the previous 3-6 months.
Exclusion of all the previous hepatitis causes
Samples enrolled in this study
Suspected DILI cases


A
ROC ALT
Sensitivity%
100% - Specificity%
B
ROC R-value
Sensitivity%
100% - Specificity%
C
ROC AST
Sensitivity%
100% - Specificity%

Received: 24 August 2021 | Accepted: 1 November 2021

DOI: 10.1111/ene.15175

european journal of neurology

ORIGINAL ARTICLE

Hepatitis E virus and Bell's palsy

Miriam Fritz-Weltin[1] | Lisa Niedermeier[1] | Estelle Frommherz[1] | Nora Isenmann[1] | Benedikt Csernalabics[2] | Tobias Boettler[2] | Christoph Neumann-Haefelin[2] | Dominique Endres[3] | Marcus Panning[4] | Benjamin Berger[1]

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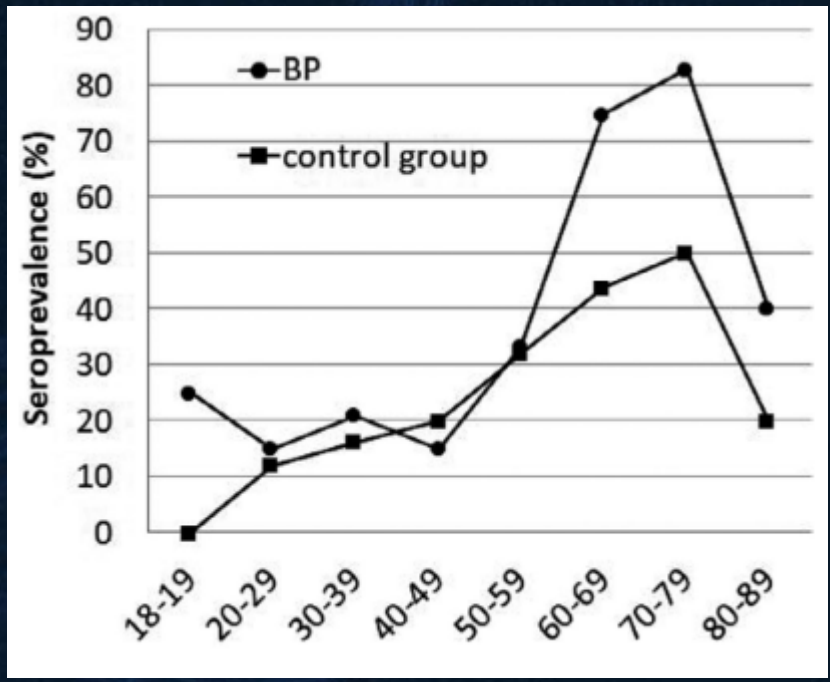
[2]Department of Medicine II, Medical Center–University of Freiburg, Faculty of Medicine, University of Freiburg, Freiburg, Germany

Abstract

Background and purpose: Acute hepatitis E virus (HEV) infections have been associated with various neurological disorders, including individual cases with Bell's palsy. Nonetheless, systematic studies in the latter are lacking. Therefore, this retrospective study systematically screened a cohort of patients with Bell's palsy for an acute HEV infection.



animals

MDPI

Article

Genetic Diversity of Hepatitis E Virus Type 3 in Switzerland—From Stable to Table

Isabelle Vonlanthen-Specker [1], Roger Stephan [2], Xaver Sidler [3], Dominik Moor [4], Cornel Fraefel [1] and Claudia Bachofen [1,*]

[1] Institute of Virology, Vetsuisse Faculty, University of Zurich, 8057 Zurich, Switzerland; isabelle.specker@outlook.com (I.V.-S.); cornel.fraefel@uzh.ch (C.F.)

cancers

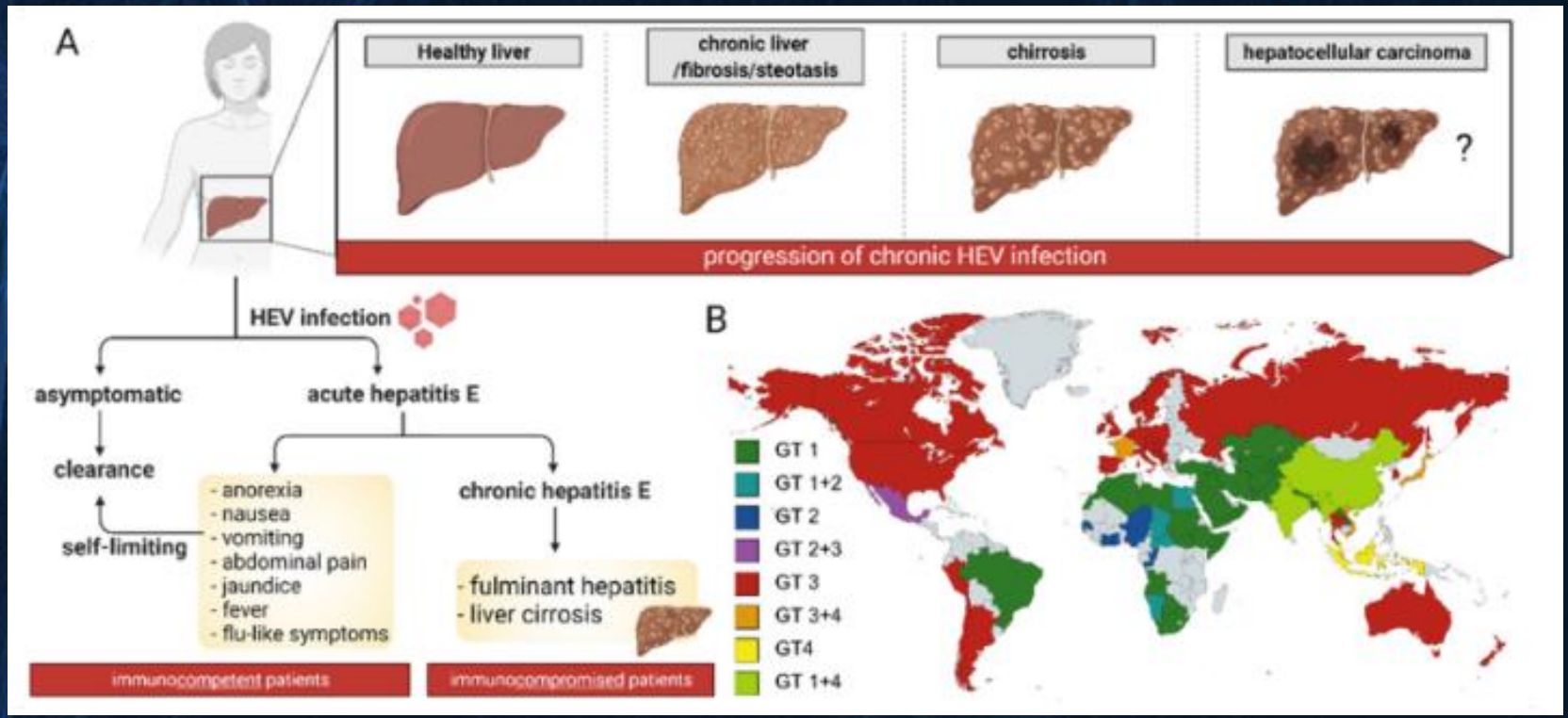
MDPI

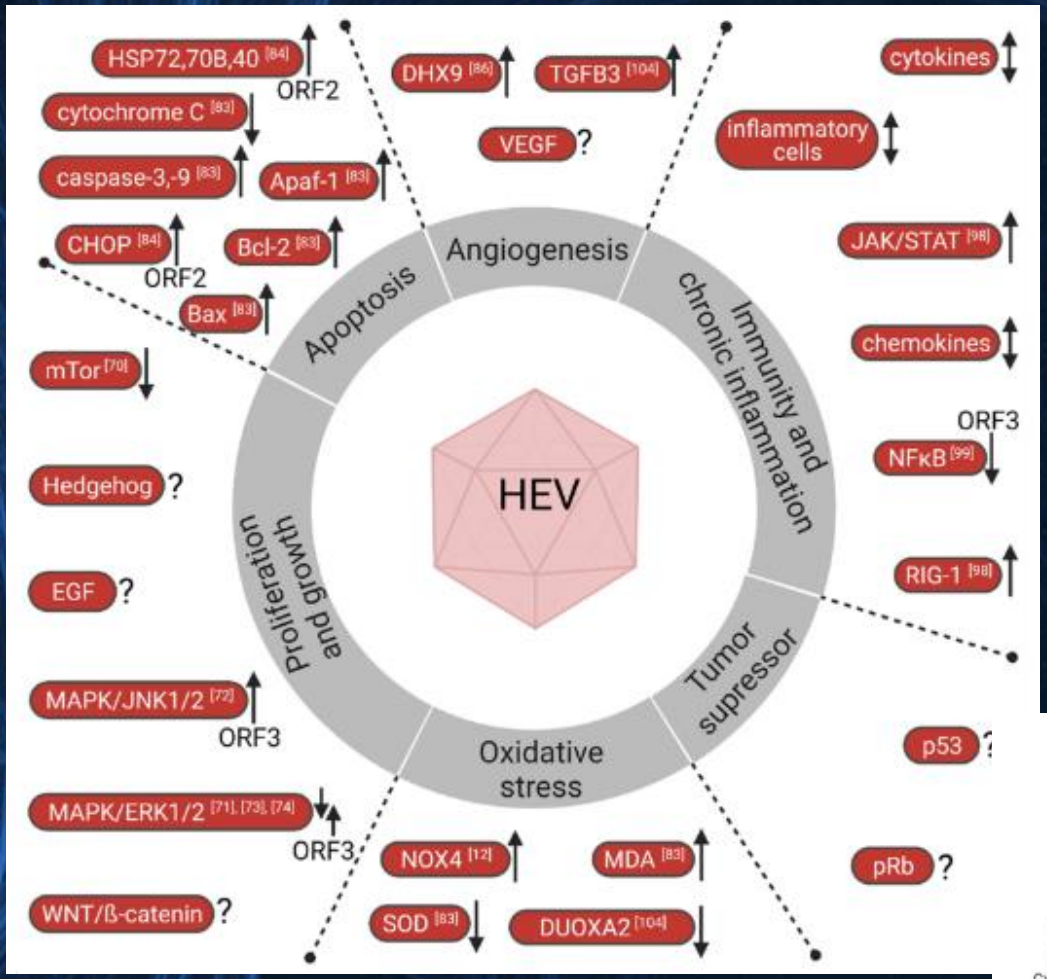
Review

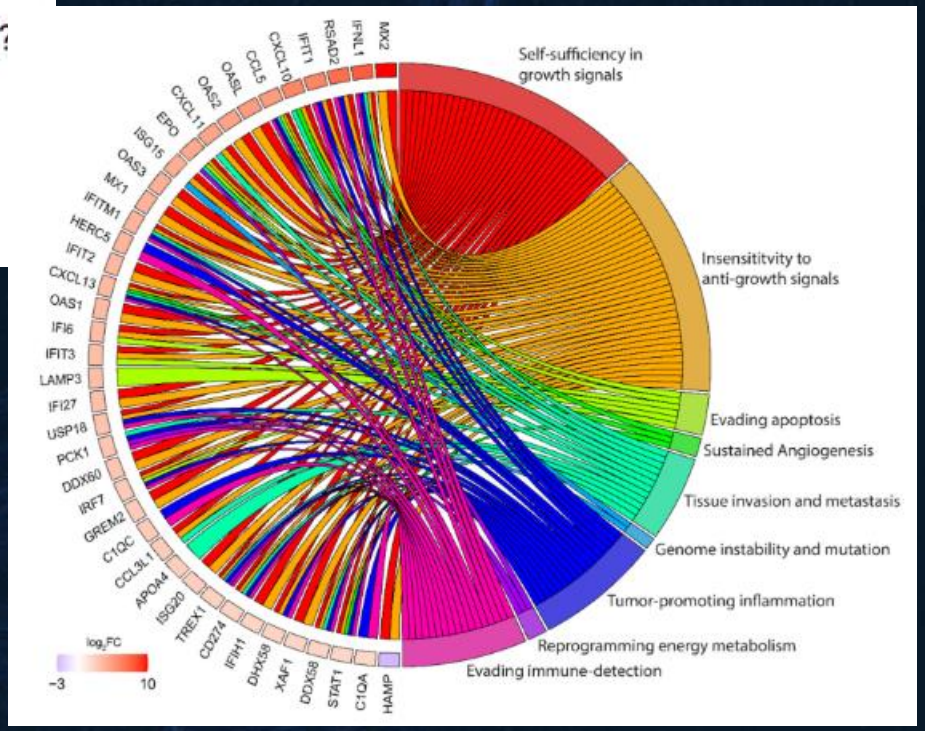
Beyond the Usual Suspects: Hepatitis E Virus and Its Implications in Hepatocellular Carcinoma

Mara Klöhn [1,†], Jil Alexandra Schrader [1,†], Yannick Brüggemann [1], Daniel Todt [1,2] and Eike Steinmann [1,3,*]

[1] Department of Molecular and Medical Virology, Ruhr-Universität Bochum, 44801 Bochum, Germany; Mara.Kloehn@ruhr-uni-bochum.de (M.K.); Jil.Schrader@ruhr-uni-bochum.de (J.A.S.);




HSP72,70B,40 [84]
ORF2
cytochrome C [83]
caspase-3,-9 [83]
Apaf-1 [83]
CHOP [84]
ORF2
Bcl-2 [83]
Bax [83]
mTor [70]
Hedgehog ?
EGF ?
MAPK/JNK1/2 [72]
ORF3
MAPK/ERK1/2 [71], [73], [74]
ORF3
WNT/ß-catenin ?
DHX9 [86]
TGFB3 [104]
VEGF ?
cytokines
inflammatory cells
JAK/STAT [98]
chemokines
ORF3
NFκB [99]
RIG-1 [98]
p53 ?
pRb ?
NOX4 [12]
MDA [83]
SOD [83]
DUOXA2 [104]
Angiogenesis
Immunity and chronic inflammation
Tumor supressor
Oxidative stress
Proliferation and growth
Apoptosis
HEV


Self-sufficiency in growth signals
Insensititvity to anti-growth signals
Evading apoptosis
Sustained Angiogenesis
Tissue invasion and metastasis
Genome instability and mutation
Tumor-promoting inflammation
Reprogramming energy metabolism
Evading immune-detection
log2FC
-3
10
MX2
IFNL1
RSAD2
IFIT1
CXCL10
CCL5
OASL
OAS2
CXCL11
EPO
ISG15
OAS3
MX1
IFITM1
HERC5
IFIT2
CXCL13
OAS1
IFI6
IFIT3
LAMP3
IFI27
USP18
PCK1
DDX60
IRF7
GREM2
C1QC
CCL3L1
APOA4
ISG20
TREX1
CD274
IFIH1
DHX58
XAF1
DDX58
STAT1
C1QA
HAMP

Brief report

Hepatitis E virus infection in hematopoietic stem cell transplant recipients: a systematic review and meta-analysis

Angkawipa Trongtorsak [1], Natapat Chaisidhivej [2], Kritika Yadav [1], Jinah Kim [3], Charat Thongprayoon [4], Wisit Cheungpasitporn [4], Panupong Hansrivijit [3]

Correspondence to Dr Panupong Hansrivijit, Department of Internal Medicine, UPMC Pinnacle Harrisburg, Harrisburg, Pennsylvania, USA; hansrivijitp@upmc.edu

Abstract

Although most patients with hepatitis E virus (HEV) infection are asymptomatic or have mild symptoms, its infection is generally underdiagnosed and overlooked. In immunocompromised patients, HEV infection can lead to acute liver failure and death. However, the clinical evidence of HEV infection in hematopoietic stem cell transplant (HSCT) recipients is scarce; thus, we conducted this systematic review and meta-analysis to assess the prevalence of HEV infection in this population. We searched

Choi *et al. BMC Infectious Diseases* (2022) 22:62
https://doi.org/10.1186/s12879-022-07050-w

BMC Infectious Diseases

RESEARCH Open Access

Acute hepatitis E virus superinfection increases mortality in patients with cirrhosis

Jung Woo Choi[1,2†], Ho Jin Son[1,3†], Sang Soo Lee[1,2,3*], Hankyu Jeon[1,3], Jin-Kyu Cho[4], Hee Jin Kim[1,2,3], Ra Ri Cha[1,2,3], Jae Min Lee[1,2,3], Hyun Jin Kim[1,2,3], Woon Tae Jung[1,2] and Ok-Jae Lee[1,2]

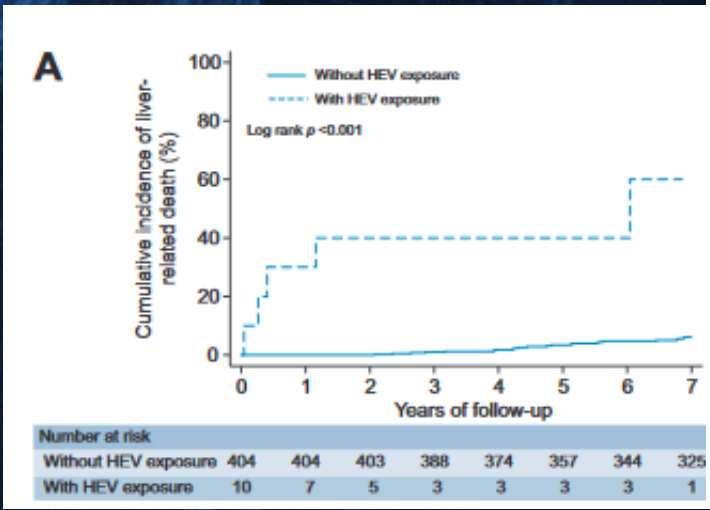
Research Article
Viral Hepatitis

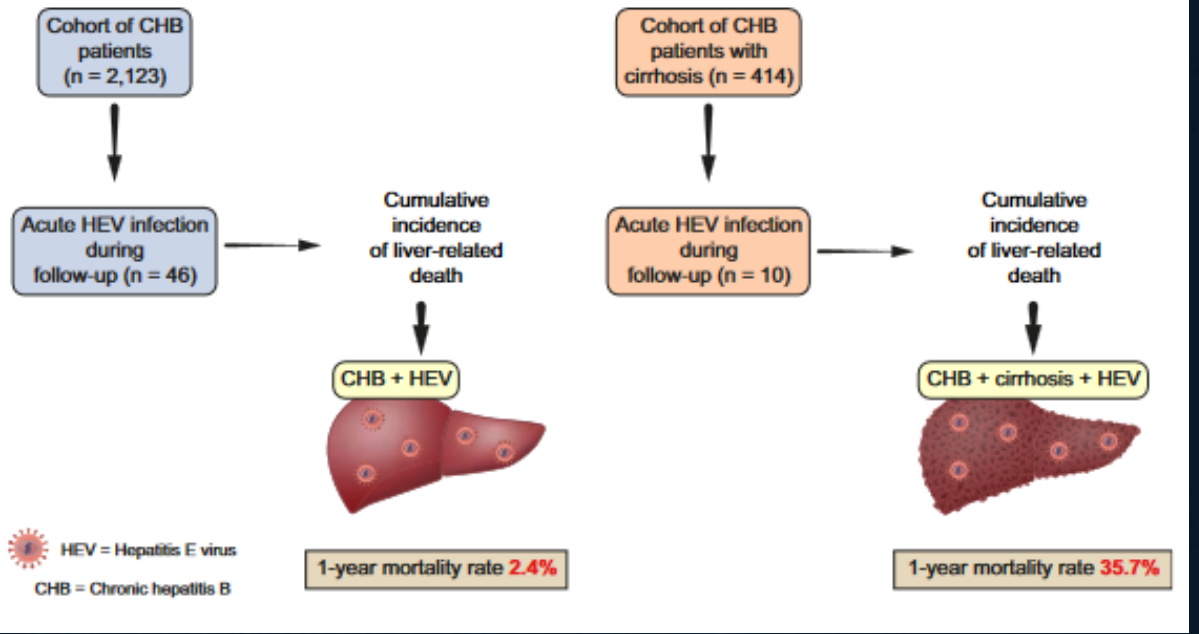
JOURNAL
OF HEPATOLOGY

HEV superinfection accelerates disease progression in patients with chronic HBV infection and increases mortality in those with cirrhosis

Tai-Chung Tseng[1,2], Chun-Jen Liu[1,2,4], Crystal T. Chang[7], Tung-Hung Su[1,2], Wan-Ting Yang[2], Cheng-Hsueh Tsai[1,2], Chi-Ling Chen[4], Hung-Chih Yang[1,4,5], Chen-Hua Liu[1,2], Pei-Jer Chen[1,2,4], Ding-Shinn Chen[1,2,4,6], Jia-Horng Kao[1,2,3,4,*]

[1]Division of Gastroenterology and Hepatology, Department of Internal Medicine, National Taiwan University Hospital, Taipei, Taiwan; [2]Hepatitis Research Center, National Taiwan University Hospital, Taipei, Taiwan; [3]Department of Medical Research, National Taiwan University Hospital, Taipei, Taiwan; [4]Graduate Institute of Clinical Medicine, National Taiwan University College of Medicine Taipei, Taiwan; [5]Department of Microbiology, National Taiwan University College of Medicine Taipei, Taiwan; [6]Genomics Research Center, Academia Sinica, Taiwan; [7]Massachusetts Institute of Technology, Cambridge, Massachusetts 02139, USA





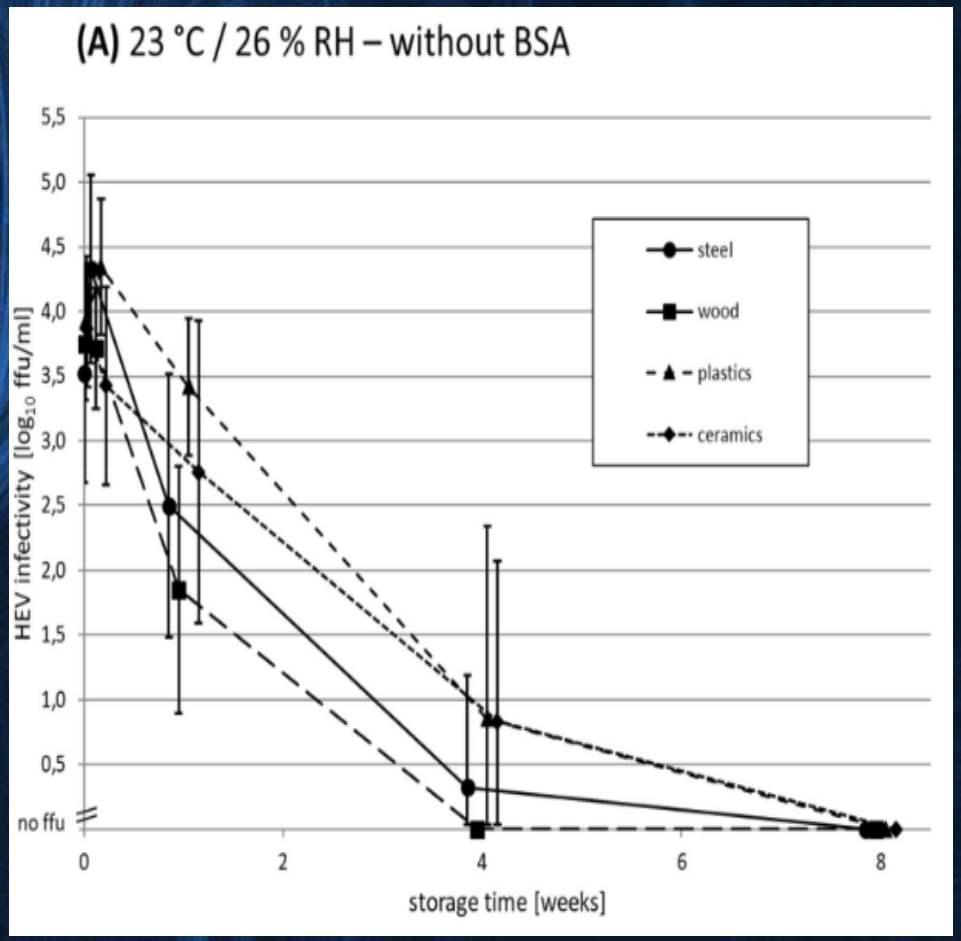
Food and Environmental Virology
https://doi.org/10.1007/s12560-022-09510-7

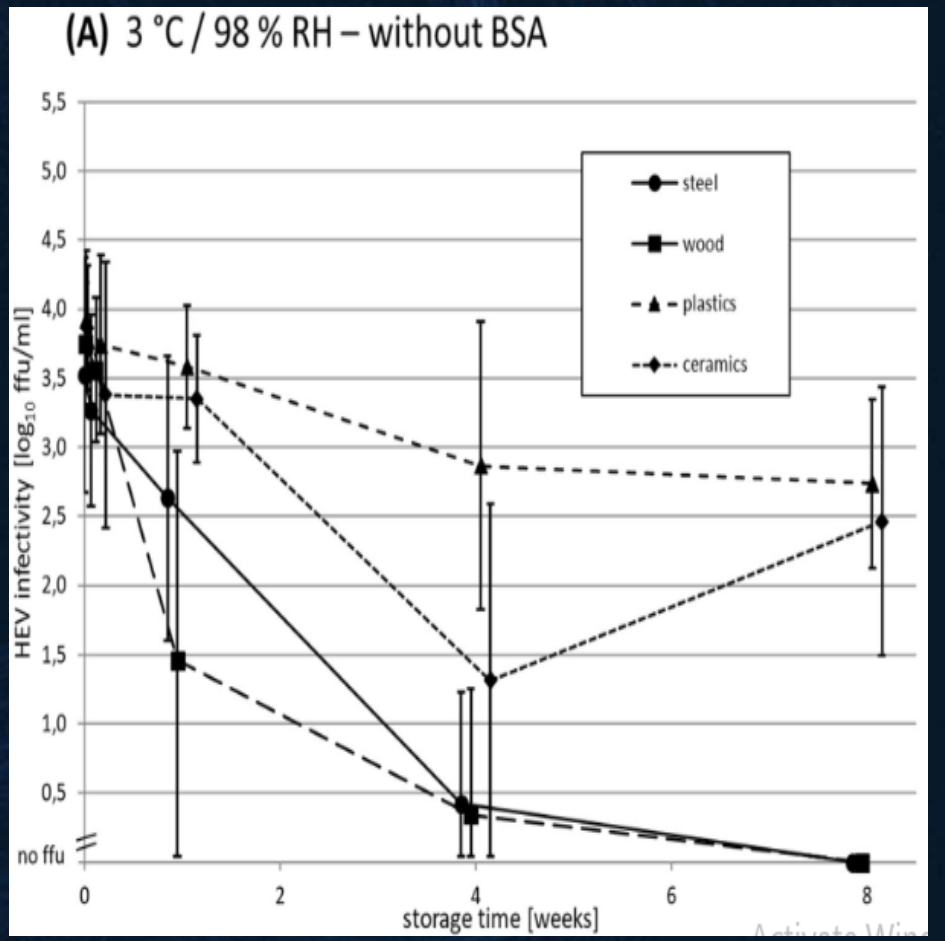
ORIGINAL PAPER

Stability of Hepatitis E Virus After Drying on Different Surfaces

Alexander Wolff[1] · Taras Günther[1] · Reimar Johne[1]

Received: 26 November 2021 / Accepted: 12 January 2022





Chronic HEV infection

- Chronic hepatitis E is defined as persistent HEV replication demonstrable by detecting HEV RNA in serum or stool three to six months following the original infection

- Chronic HEV is believed to be exclusive to immunosuppressed and immunocompromised patients. The immunosuppressed patients are those on immunosuppressive
- agents due to either solid organ transplant (SOT) or those on chemotherapy for haematological malignancies

Laboratory diagnosis

- Numerous methods are available for detecting HEV both direct and indirect.
- These methods include immune electron microscopy (IEM), fluorescent antibody blocking assay, Enzyme Immunoassay (EIA), immunoblot (IB), immunochromatography, and reverse –transcription polymerase chain reaction (RT-PCR)

- ELISA HEV antibodies of IgM and IgG class
- The specificity and sensitivity of these different assays range from about 40 to more than 90% for different genotypes and geographic locations

Treatment

- Hepatitis E virus infection treatment depends on the outcome of the infection. For acute viral hepatitis in immunocompetent individuals, viral clearance is usually spontaneous. Thus, this group of patients may require only supportive and symptomatic treatment.
- However, in the case of severe HEV infection in immunocompetent persons, treatment with ribavirin at 1200 mg/day for 21 days is recommended
- Although, for acute liver failure by HEV infection in pregnancy, the major form of treatment is supportive intensive care (ribavirin has a teratogenic effect)

Treatment

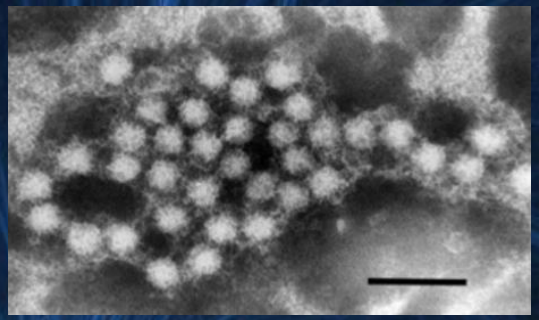
- It is also recommended that patients with acute HEV infection awaiting transplant or undergoing haemodialysis should be treated.
- A short course (10 days to 3 months) of ribavirin (at 200 mg – 1000 mg/day) should be given before the transplant (Péron, 2011).
- While pegylated interferon-alpha (at 135 mg/week) for three months is used for the haemodialysis patients.

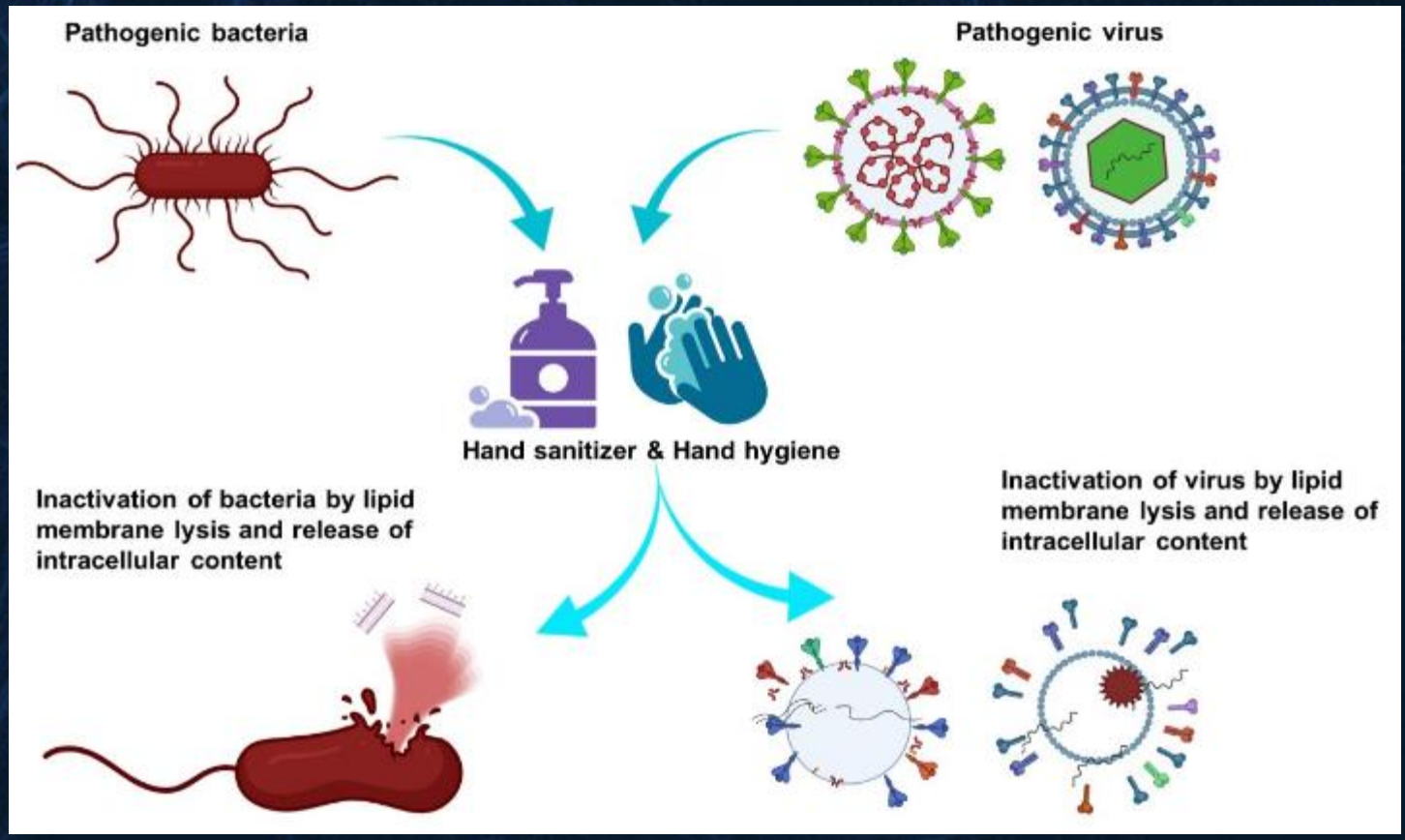
Vaccine

- Good basic hygiene although effective in the prevention of hepatitis E, is not all-encompassing. Since it does not suffice for other sources of transmission beyond waterborne and foodborne routes.
- Thus, the safest and most effective means of HEV prevention and control should be through vaccination. Of the numerous vaccine candidates, two were outstanding and underwent human clinical trials

Vaccine

- A baculovirus – expressed 56 KDa protein and an E. coli – expressed HEV 239 protein.
- The 56 KDa protein though yet to be licenced, has gone through both phase I and II human clinical trials. On the other hand, the HEV 239 vaccine has its efficacy evaluated in phase III double – blind, a randomized clinical survey conducted in China. The vaccine has the following advantages:
- cross – protection against other HEV genotypes.
- Potential for rapid control vaccination during epidemics.
- Hence, the vaccine was licenced for use in China in 2012 under the brand name Hecolin. However, the vaccine is yet to be approved by any other country aside China.




Pathogenic bacteria
Pathogenic virus
Hand sanitizer & Hand hygiene
Inactivation of bacteria by lipid membrane lysis and release of intracellular content
Inactivation of virus by lipid membrane lysis and release of intracellular content

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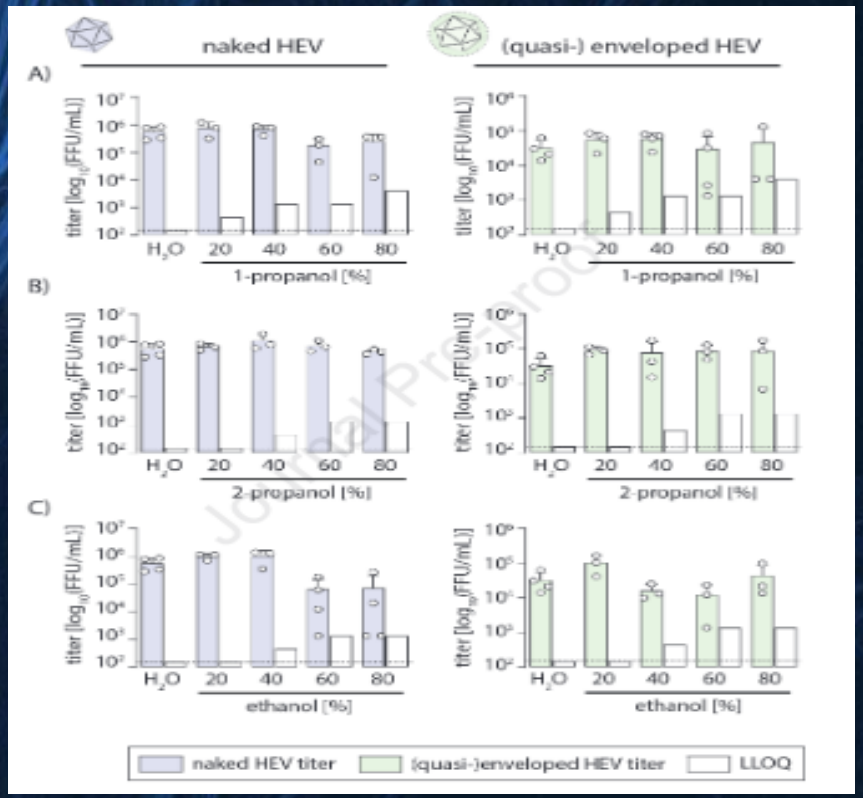
FULL LENGTH ARTICLE | ARTICLES IN PRESS

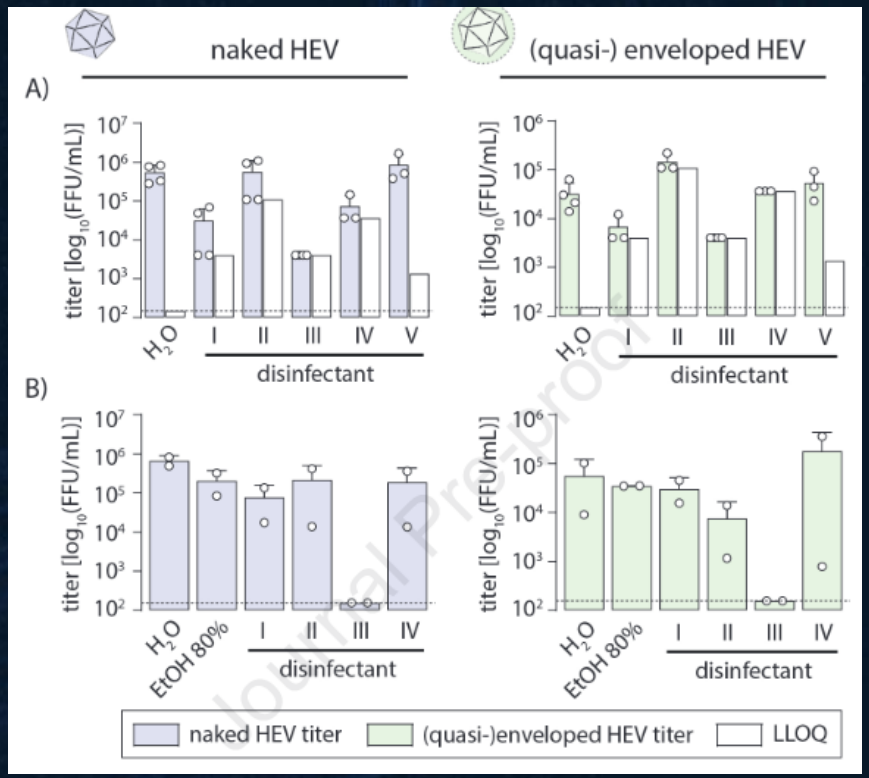
PDF [12 MB]

Hepatitis E virus is highly resistant to alcohol-based disinfectants

Patrick Behrendt # • Martina Friesland # • Jan-Erik Wißmann • ... Heiner Wedemeyer • Daniel Todt • Eike Steinmann • Show all authors • Show footnotes

Open Access • Published: January 24, 2022 • DOI: https://doi.org/10.1016/j.jhep.2022.01.006





Conclusion

- Hepatitis E virus as a pathogen has evolved since its discovery.
- The pathogen is now known for causing a disease that is globally distributed with an increased public health challenge
- The risk factors for HEV infection have also increased due to its multiple means of transmission. Of interest are zoonotic transmission, blood-borne transmission, and to a lesser extent vertical transmission.
- As a result, more populations are at risk of HEV infection now than ever.

Thanks for your attention