Corso
Precongressuale
Le infezioni da non dimenticare nel paziente trapiantato

Virus dell'Epatite E

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XLVI Congresso Nazionale AMCLI
11 - 14 Novembre 2017
Palacongressi di Rimini

Outline

- Introduction to HEV
- Contexts of HEV acquisition in transplant
- Impact of immune suppression on clinical evolution
- How to study HEV prevalence/incidence
- Clinical management (therapeutic options)

Every year there are 20 million hepatitis E infections, over 3 million acute cases, and 70,000 hepatitis E-related deaths.

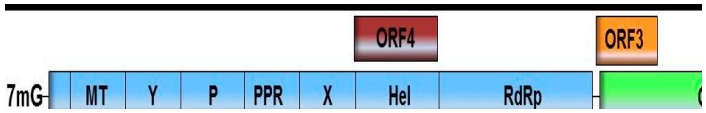
SCIENTIFIC OPINION 2017

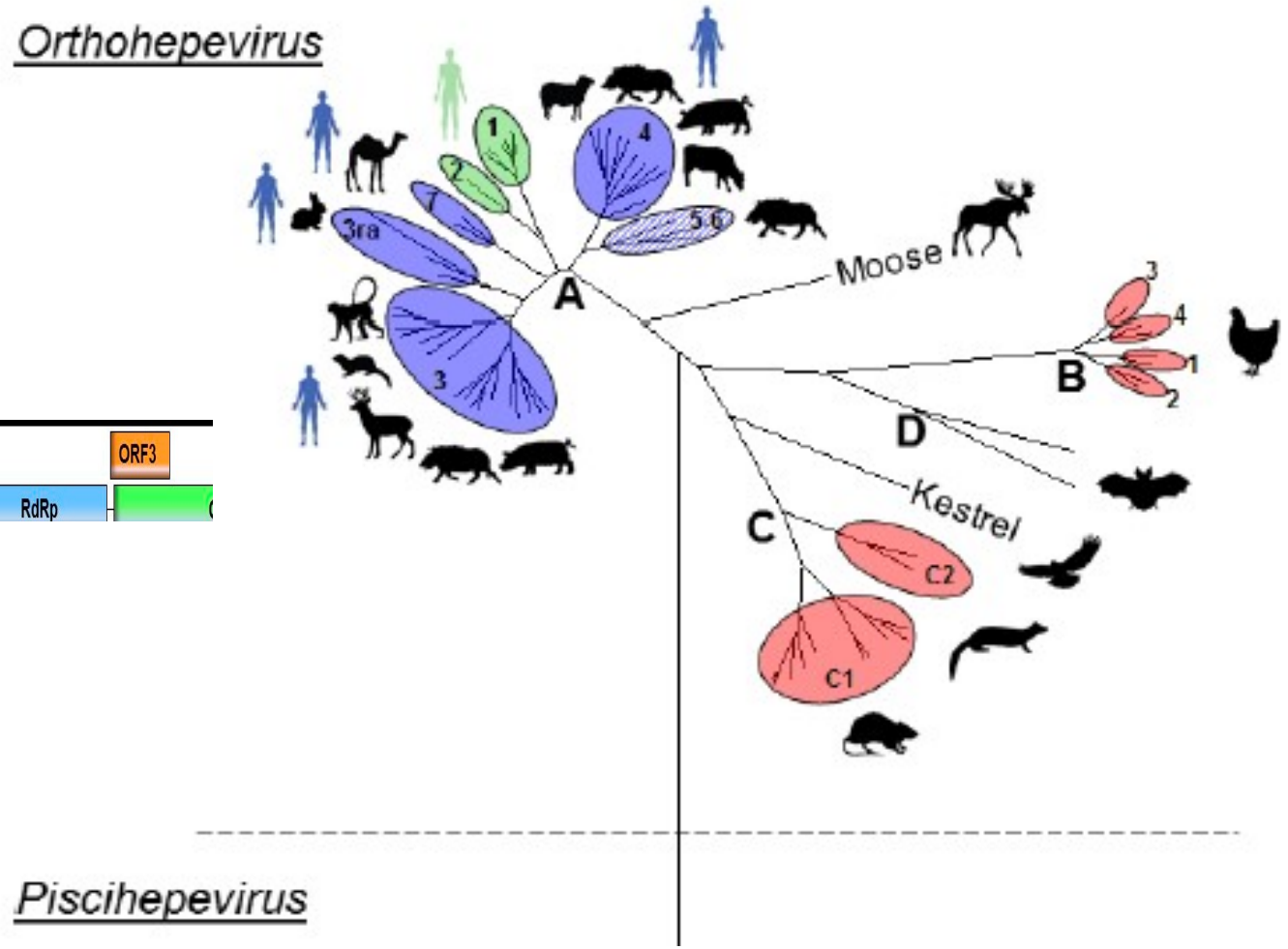
Public health risks associated with hepatitis E vir

Family *Hepeviridae*

Two genera: Orthohepevirus
Piscihepevirus

Genome 7.2 Kb





Worldwide distribution of hepatitis E virus

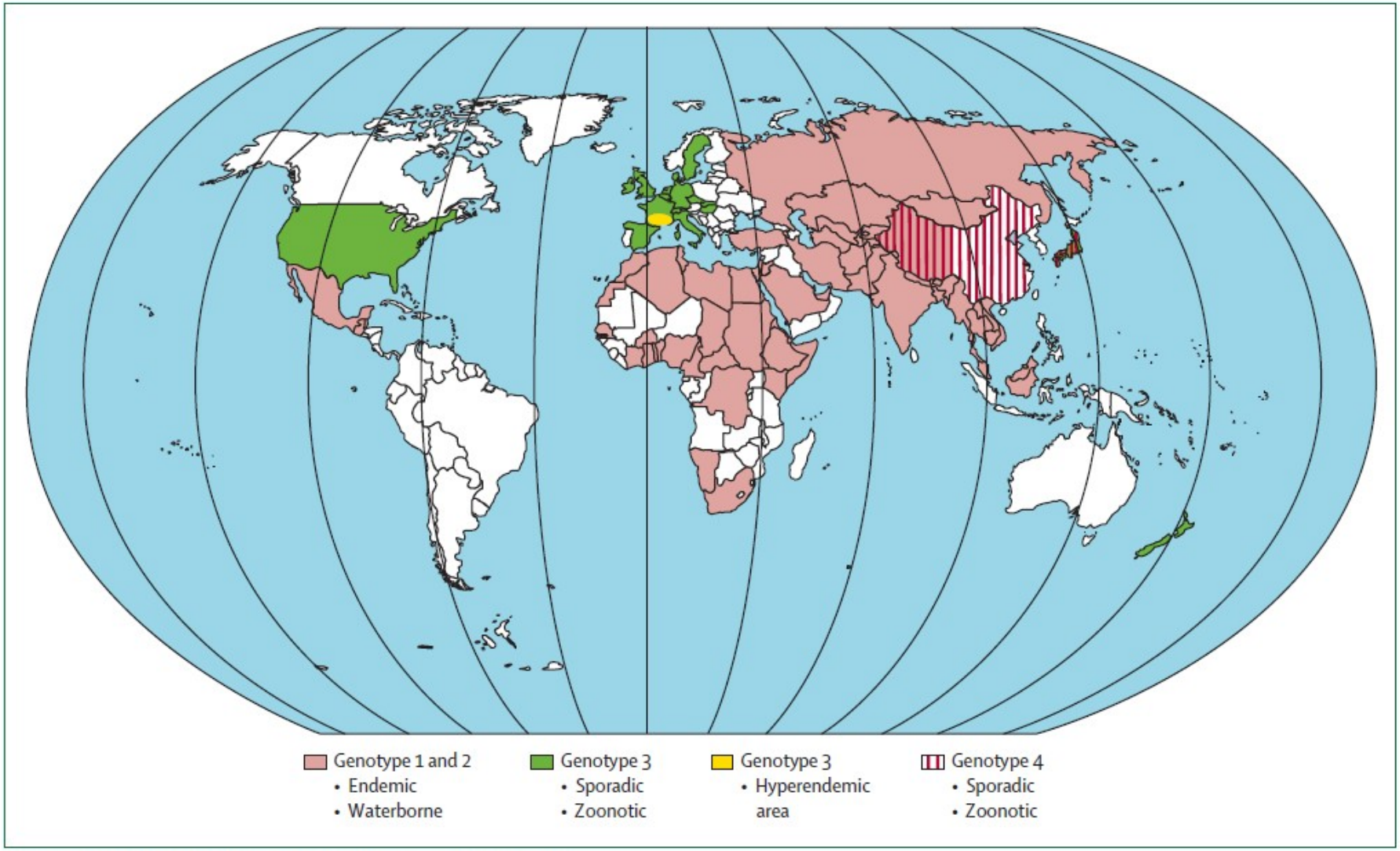
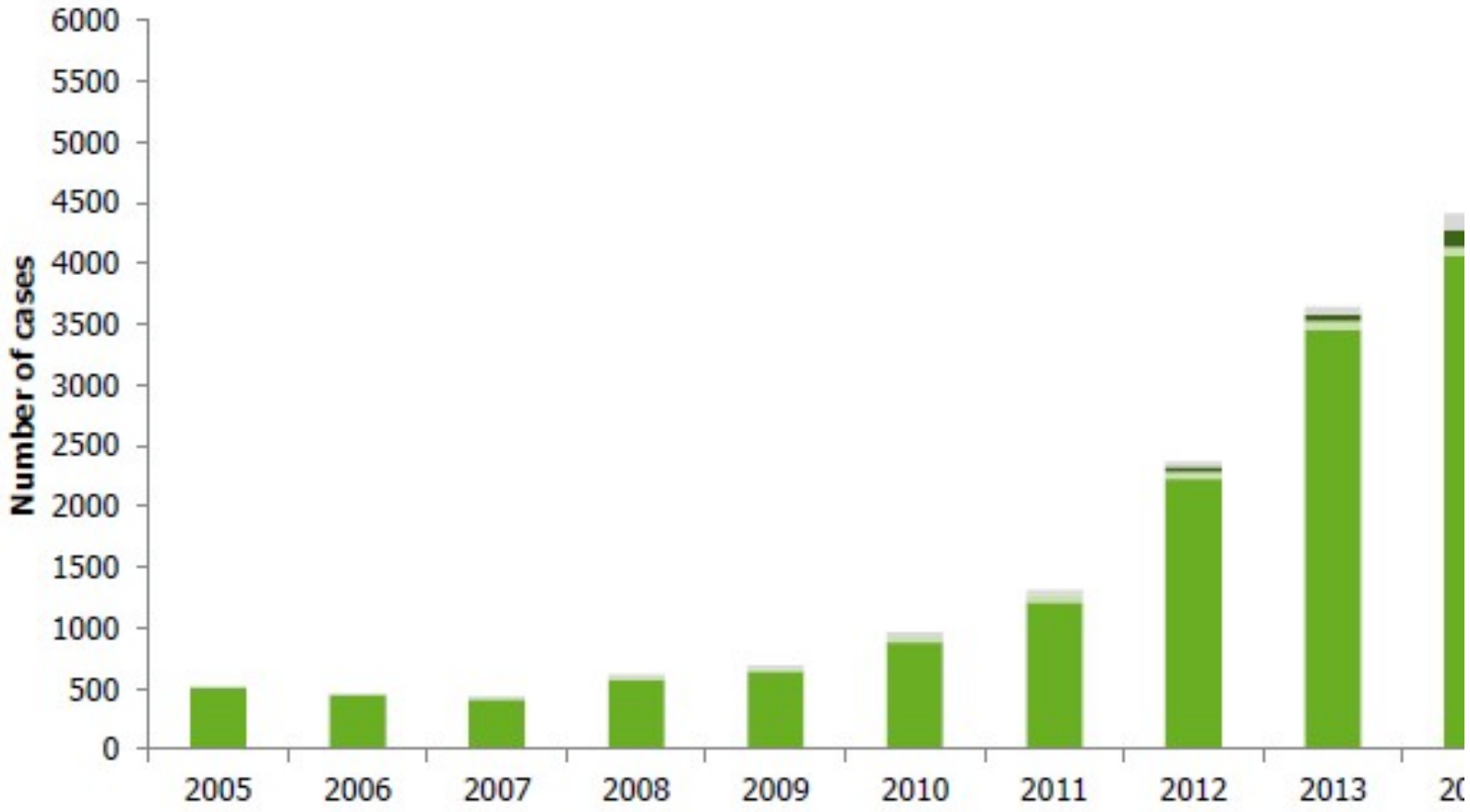


Figure 2: **Worldwide distribution of clinical cases of HEV infection**
Note, that in several countries, including in South America, there have been occasional reports of HEV3 infection. Countries left blank are those with insufficient data.

Kamar et al. Lancet 2012

Hepatitis E in the EU/E
2005–2
Baseline assessment of testing, diag
surveillance and epidem

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



Hepatitis E in the EU/E
2005–2
Baseline assessment of testing, diag
surveillance and epidem

Figure 3.9. Hepatitis E associated with blood and/or blood product transfusion, States, 2005–2015*

Developing countries

- HEV1-HEV2
- Epidemic
- High Deaths in pregnancy (25%)
- Extra-hepatic disease
- Chronic infection not reported
- Waterborne, person to person (?)

Developed countries

- HEV3-HEV4
- Sporadic, authoctonous, small cluster
- Deaths in pregancy not reported
- Extra-hepatic disease
- Chronic infection reported (HEV-3, HIV..)

Annual incidence estimates:

0.2% in UK (Ijaz S, J Clin Virol 2009)

0.7% in US (Faramawi MF, Epidemiol Infect 2011)

4.3% in China (Li RC, Emerg Infect Dis 2006)

2.1% in South France (Abravanel F, JID 2014)

J Gen Virol (2011), DOI 10.1099/vir.0.031278-0

other

Hepatitis E Virus In Italy: Molecular Analysis Of Travel-Related And Autochthonous Cases

Giuseppina La Rosa[1,3], Michele Muscillo[1], Valentina Spuri Vennarucci[1], Anna Rosa Garbuglia[2], Patrizia La Scala[2] and Maria Rosaria Capobianchi[2]

[1] Istituto Superiore Sanita, Roma;
[2] National Institute for Infectious Diseases 'L. Spallanzani', Rome, Italy

Human HEV infection in Italy is caused by different genotypes, depending on whether the infection is travel-related (gen 1) or autochthonous (gen 3).

Rare and Emerging Viral Infect
Transplant Recipients

Clinical Infectious Diseases Advance Access published

Table 1. Rare and Emerging Viral Infections in the Transplant Population: Case Series or Multiple Cases Report

Virus	Virus Family	Transplant	Clinical Manifestations	
HTLV-1	*Retroviridae*	SOT and HSCT; donor-derived infections reported	Adult T-cell leukemia and HTLV-1–associated myelopathy	Associat after H
HEV	*Hepeviridae*	SOT predominantly; case report in HSCT	Chronic viremia, elevated LFTs, cirrhosis; rare reports of neurological complications	Typically treatm reduce peg-in
Rabies	*Rhabdoviridae*	SOT, ileac artery graft, cornea transplants; all cases donor derived	Fatal encephalitis; cornea transplants present with pain in eye with graft	Survivors transp liver tr vaccin
LCMV and novel arenavirus	*Arenaviridae*	SOT; all reported cases donor derived	Fever, abdominal pain, nausea, vomiting, diarrhea, altered mental status; often peri-incisional rash and tenderness	14 of 17 emplo cornea
Measles	*Paramyxoviridae*	SOT and HSCT	Occasional clinical measles; SME (afebrile, altered mental status, intractable seizures); interstitial pneumonia	SME fata patien severe minori recipie
Mumps	*Paramyxoviridae*	SOT and HSCT	Parotitis, orchitis, vestibular neuronitis, and renal allograft involvement (SOT); fatal encephalitis (HSCT)	3 cases i patien encep post-H
Dengue	*Flaviviridae*	SOT and HSCT	Dengue fever; severe dengue, including hemorrhagic fever and shock	Dengue high m dengu

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The first case of HEV infection in a KTR was reported in 2003 in India (Sinha et al., Clinical Transplantation 2003)

Acute pancreatitis following kidney transplantation – role of viral infec

Clin Transplant 2003: 17: 32

HEV and the transplant setting

1. Pre-transplant (fulminant hepatitis requiring liver transplantation)
2. Acquired with transplanted organ (liver??)
3. Acquired in the post-transplant
4. Reactivation of a previously resolved infection

TABLE 2 Results of investigation performed for
and transplant workup in our patient

Tests performed	Results (refer
HBsAg	Negative
Anti-HBs	<10
Anti-HBc (Total)	Negative
HBV DNA viral load	<10 IU/mL
Anti-HAV Ab (total)	Positive
Anti-HAV IgM	Negative
Anti-HEV (total)	Positive
Anti-HEV IgM	Positive
Anti-HIV-1	Negative
Antibody titer	
CMV IgG	Positive
EBV-VCA polyvalent	640
HSV	Anti-complem
Hantavirus polyvalent	<40
Widal test (TO, TH, AH, BH, CH)	<1:50
Leptospira IgM	Negative
Bacterial culture	
Blood, sputum and urine	No growth
Immunoglobulin levels	
IgG	21.80 (7.00-1
IgA	5.15 (0.70-4.
IgM	2.82 (0.40-2.
Autoimmune markers	
C3	46 (76-150) r
C4	14 (9-35) mg
ANA titer	Negative
Anti-ENA screen	Negative
Anti-smooth muscle Ab	Negative

Acute hepatitis E virus infection causing acute liver requiring living-donor liver transplantation in a non immunocompetent woman

Iris Wai Sum Li[1,2] | Kenneth Siu Ho Chok[3]

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[2]School of Public Health, The University of Hong Kong, Hong Kong, China
[3]Department of Surgery, The University of Hong Kong, Hong Kong, China

Correspondence
Iris Wai Sum Li, Queen Mary Hospital, Hong Kong, China.

Abstract

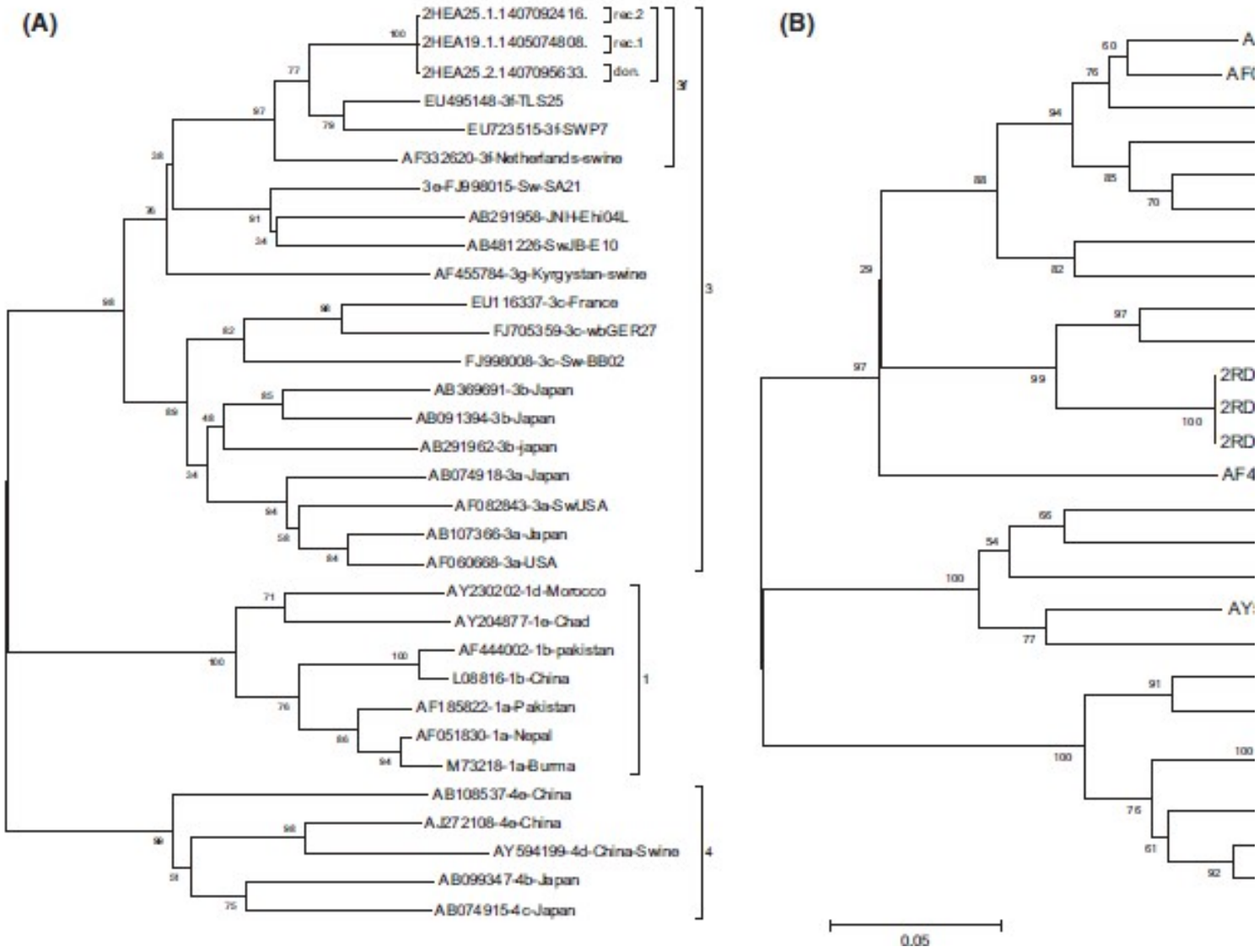
We report a rare case of acute liver failure from acute hepatiti
pregnant woman without comorbidities who survived after li
source was likely consumption of partially cooked pig liver.
second most common genotype causing acute hepatitis E i
Fulminant hepatitis E rarely occurs without a risk factor, as

Wai Sum Li I. et al. Transpl Infect Dis. 2017

Received: 11 February 2016 | Revised: 26 April 2016 | Revised: 7 July 2016 | Revised: 23 August 2016 | Accepted: 9 Sept
DOI: 10.1111/tid.12624

CASE REPORT

Evidence of hepatitis E virus transmission by renal g



Centro Nazionale Trapianti

Ultima revisione 9 agosto 2012

Criteri generali per la valutazione di idoneità del donatore

ALLEGATO B
Valutazione di idoneità del donatore

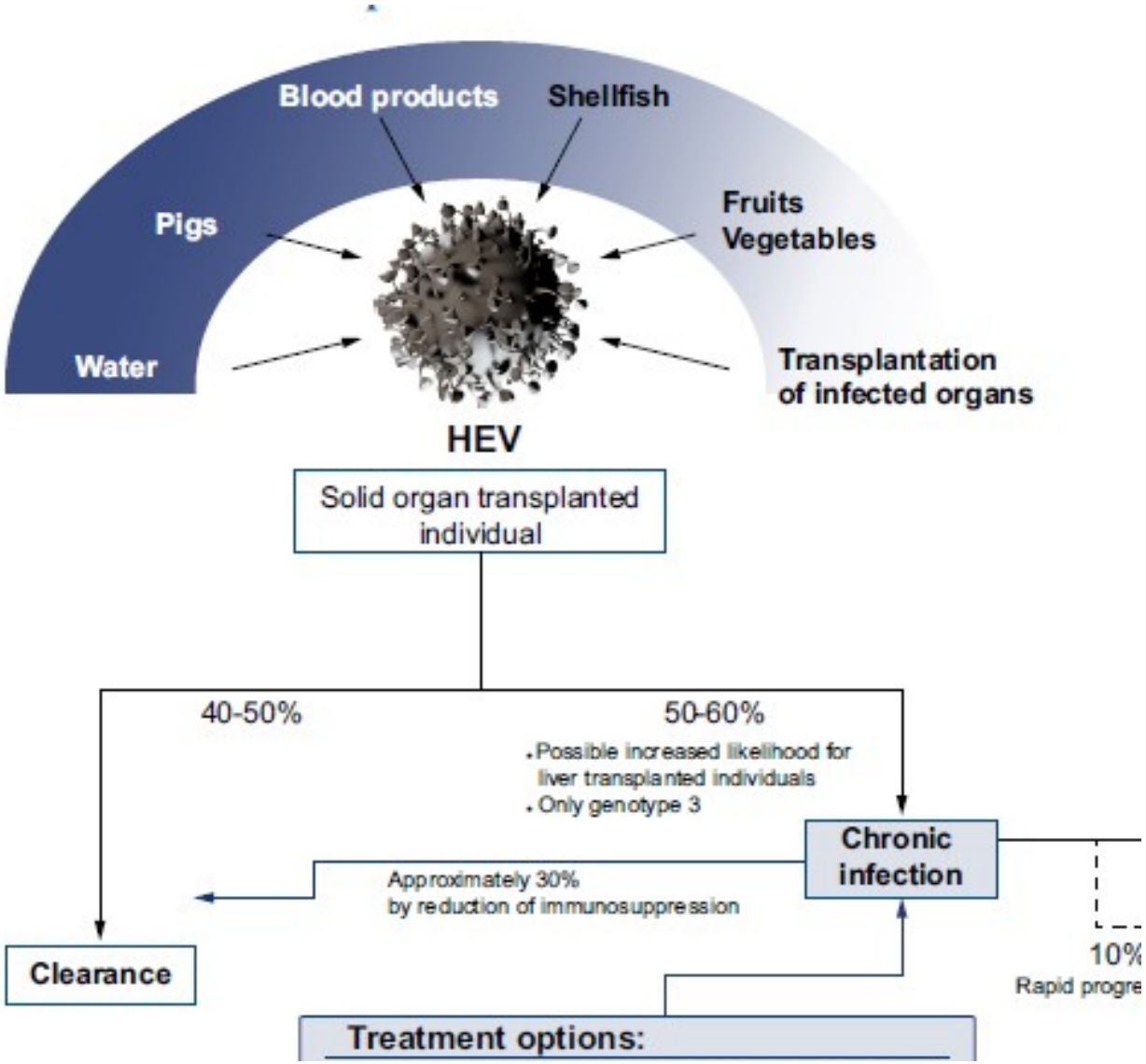
Indagini biomolecolari supplementari da effettuare a donatori per i quali l'anamnesi, l'esame obiettivo o i risultati di esami di laboratorio facciano emergere dubbi:

HIV-RNA e/o
HCV-RNA e/o
HBV-DNA
HEV-RNA

- *Ricerca anticorpi di classe IgG e IgM e RNA di West Nile Virus per i donatori provenienti da aree endemiche stagionali indicate annualmente dal Centro Nazionale Trapianti*
- *Ricerca anticorpi di classe IgG e IgM e RNA di West Nile Virus per i donatori provenienti da aree endemiche non stagionali indicate dal Centro Nazionale Trapianti*
- *Test sierologici per Chagas nei donatori provenienti da aree endemiche (vedi All. E).*

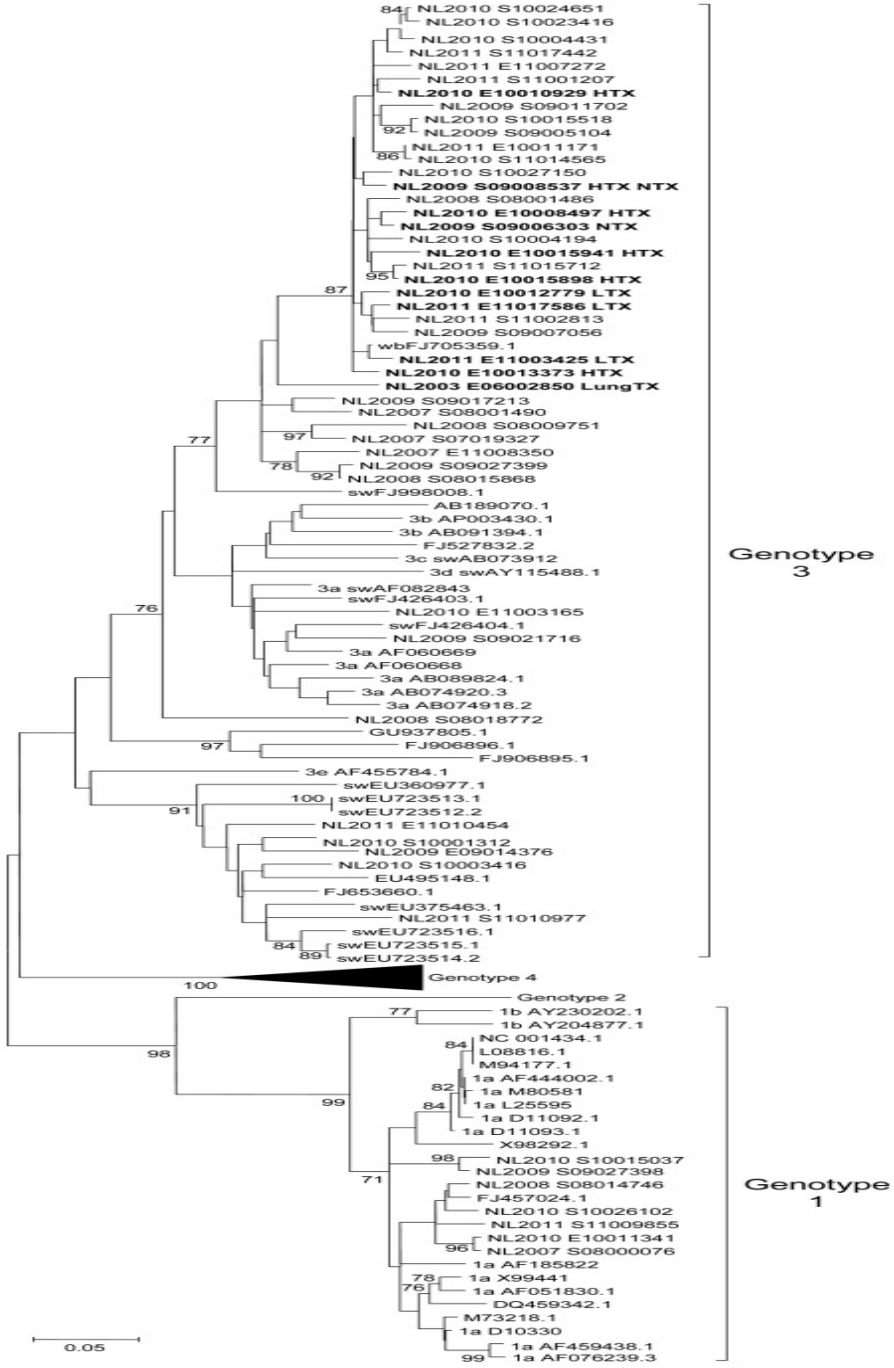
Journal of Hepatology **2014** vol. 61 | 141

Transmission and disease progression in SOT



Boldface indicates virus strains of chronic HEV-infected solid organ transplant recipients identified in this study.

Viruses isolated from samples from 11 chronic HEV-infected solid organ transplant recipient were all genotype 3



Pas S et al. Emerg Infect Dis. 2012

Genome Announc. 2017 May 18;5(20)

Identification of a Novel Hepatitis Virus Genotype 3 Strain Isolated fr Chronic Hepatitis E Virus Infection Kidney Transplant Recipient in Switzerland

Bo Wang,[a] Dominik Harms,[a] Jörg Hofmann,[b,c] Diana Ciardo,[d] Agne
C.-Thomas Bock[a]

Department of Infectious Diseases, Robert Koch Institute, Berlin, Germany[a]; Institute of Medi
Charité University Medicine, Berlin, Germany[b]; Labor Berlin, Charité-Vivantes GmbH, Berlin, G
Immunology, Viollier AG, Allschwill, Switzerland[d]; Department of Internal Medicine/Nephrol
Lachen, Switzerland[a]

ABSTRACT Hepatitis E virus genotype 3 (HEV-3) is the causal patho

Accession number(s). The complete genome sequence of SW/16-
deposited in GenBank under the accession number KY780957.

Solid organ transplant (SOT) ed HEV

Le modalità di trasmissione dell' epatite E in soggetti sottoposti a trapianto sono le medesime descritte per la popolazione generale.

Il consumo di carne di maiale poco cotta o salumi rappresentano la principale fonte di infezione. Tuttavia possiamo avere anche una riattivazione di infezioni pregresse.

Il 60% dei soggetti che hanno subito trapianto di organo, se esposti al virus HEV, sviluppano **epatite cronica**.
Il **10%** di essi va verso la **cirrosi** in due anni.

Blood
bloodjournal.hematologylibrary.org

Published online before print June 21, 2013, doi: 10.1182/blood-2013-03-492363
Submitted: March 26, 2013 Accepted: June 14, 2013
Blood August 8, 2013 vol. 122 no. 6 1079-1086

Hepatitis E virus: an underestimated opportunistic pathogen in recipients of allogeneic hematopoietic stem cell transplantation

Jurjen Versluis[1], Suzan D. Pas[2], Hendrik J. Agteresch[1,3], Robert A. de Man[4], Jolanda Maaskant[2], Marguerite E. I. Schipper[5], Albert D. M. E. Osterhaus[2], Jan J. Cornelissen[1], and Annemiek A. van der Eijk[2]

- High probability of developping chronic hepatitis
- HEV to be included in differential diagnosis pf ALT elevation in HSCT

transplantation (alloHSCT). Therefore, we set out to study the incidence and sequelae of HEV as a cause of hepatitis in a recent cohort of 328 alloHSCT recipients. HEV RNA was tested in episodes of liver enzyme abnormalities. In addition, HEV RNA and HEV serology were assessed pre- and post-alloHSCT. We found 8 cases (2.4%) of HEV infection, of which 5 had developed chronic HEV infection. Seroprevalence pre-alloHSCT was 13%. Four patients died with HEV viremia, with signs of ongoing hepatitis, having a median time of infection of 4.1 months. The 4 surviving patients cleared HEV after a median period of 6.3 months. One patient was diagnosed with HEV reactivation after a preceding infection prior to alloHSCT. Although the incidence of developing acute HEV

EMERGING INFECTIOUS DISEASES®

Pas S et al. Emerg Infect Dis. 2012

Hepatitis E Virus Infection among Solid Organ Transplant Recipients, the Netherlands

This immunocompromised population is at risk for chronic hepatitis E virus infection

1,200 patients SOT recipients screened for HEV infection in Netherlands:

✓Screening by PCR .

✓In 12 (1%) patients, HEV detected

✓in 11/12 chronic infection developed.

		HEV infections, no. (%	
ıp	No. recipients	Confirmed	Chroni
Heart			
Lung	259	5 (1.9)	5 (1.9)
Liver	53	1 (1.9)	1 (1.9)
Kidney	300	3 (1.0)	3 (1.0)
Multiple	574	1 (0.2)	1 (0.2)
Multiple SOT†	14	2 (14.3)	1 (7.1)

Journal of Clinical Virology 69 (2015) 22–26

Contents lists available at ScienceDirect

Journal of Clinical Virology

journal homepage: www.elsevier.com/locate/jcv

Paediatric liver transplanted patients and prevalence of hepatitis E virus

- In France, HEVseroprevalence in liver or liver+kidney pediatric recipients is 8.3%, in line with other studies
- In 50% seroconversion after transplant
- No correlation with immunosuppressive therapy
- No chronic cases observed

Prevelence of HEV IgG antibodies and immunosuppression by age group.

Group (yr)	Number of patients	Type of transplantation LT-LKT	Mean time post-transplantation ± 2SD (range)	Male–female	Anti-HEV IgG positive (*n*(%))
<5	9	7–2	2.4 ± 154(0.9–3.7)	4–5	0(0%)
5–10	32	30–2	4.8 ± 3.9(1.2–8)	15–17	4(12.5%)
10–15	25	21–4	8.3 ± 7(1.2–12.9)	13–12	1(4%)
15–20	22	21–1	13.1 ± 9.7(2–18)	8–14	2(9.1%)

Outline

- Introduction to HEV
- Contexts of HEV acquisition in transplant
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- Clinical management (therapeutic options)

Chronic HEV involves several transplant types, not only liver

Factors Associated With Chronic Hepatitis in Patients W[illegible] E Virus Infection Who Have Received Solid Organ Transp[lant]

NASSIM KAMAR,[*,†,§] CYRIL GARROUSTE,[*,‖] ELIZABETH B. HAAGSMA,[¶] VALÉRIE GARRIGUE
CÉCILE CHAUMET [‡‡] JÉROME DUMORTIER [§§] AMÉLIE CANNESSON [‖‖] ELISABETH CASSUTO

Table 1. Type of Organ and Reason for Transplant in Solid Organ Transplant Recipients With Autochthonous HEV Infection

Type of organ transplant	n	Reason for transplant
Kidney	47	Glomerular disease
		Genetic disease
		Uropathy and interstitial nephropat
		Vascular disease and diabetes
		Unknown
Liver	26	Chronic viral hepatitis
		• Hepatitis B virus (n = 4)
		• Hepatitis C virus (n = 3)
		• Hepatitis C virus/HIV (n = 1)
		Alcohol-related liver disease
		Genetic disease
		Autoimmune hepatitis
		Other causes
Liver-kidney	2	Alcoholic liver disease/chronic ren disease
		Idiopathic portal hypertension/ chronic renal disease
Kidney-pancreas	6[a]	Type 1 diabetes mellitus
Islet cell	1	Type 1 diabetes mellitus
Heart	2	Ischemic heart disease

Table 2. HEV Serologic and PCR Results at Diagn[osis] Solid Organ Transplant Patients With HE[V]

HEV diagnostic test	No. tested	No. positive
Anti-HEV IgM[a]	78	32
Anti-HEV IgG[a]	78	63
Serum HEV PCR	82[b]	82
HEV genotyping	64	59[c]

[a]A wide range of differing commercial and in-house assays and these differed from center to center.
[b]Three patients were not tested for HEV RNA by PCR. The HEV infection in these cases was based on an increased level.
[c]All 59 patients in whom HEV was genotyped were infect[ed] genotype 3. In 50 of these cases, HEV subtyping was pe[rformed]

Transplant I

Case report

Hepatitis E virus: an underdiagnosed cau
chronic hepatitis in renal transplant recip

D. Halleux, N. Kanaan, B. Kabamba, I. Thomas, Z. Hassoun.
Hepatitis E virus: an underdiagnosed cause of chronic hepatitis in renal transplant recipients
Transpl Infect Dis 2012: **14**: 99–102. All rights reserved

Abstract: Hepatitis E virus (HEV) infection can evolve to chronic hepatitis in immunocompromised patients leading to rapidly progressive cirrhosis. Proper diagnosis is therefore important, as

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I. Thomas[3], Z. Hasso

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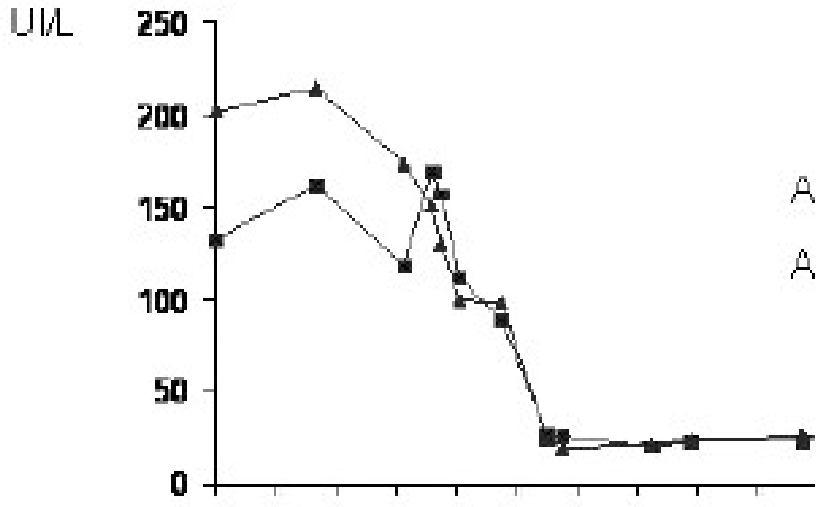
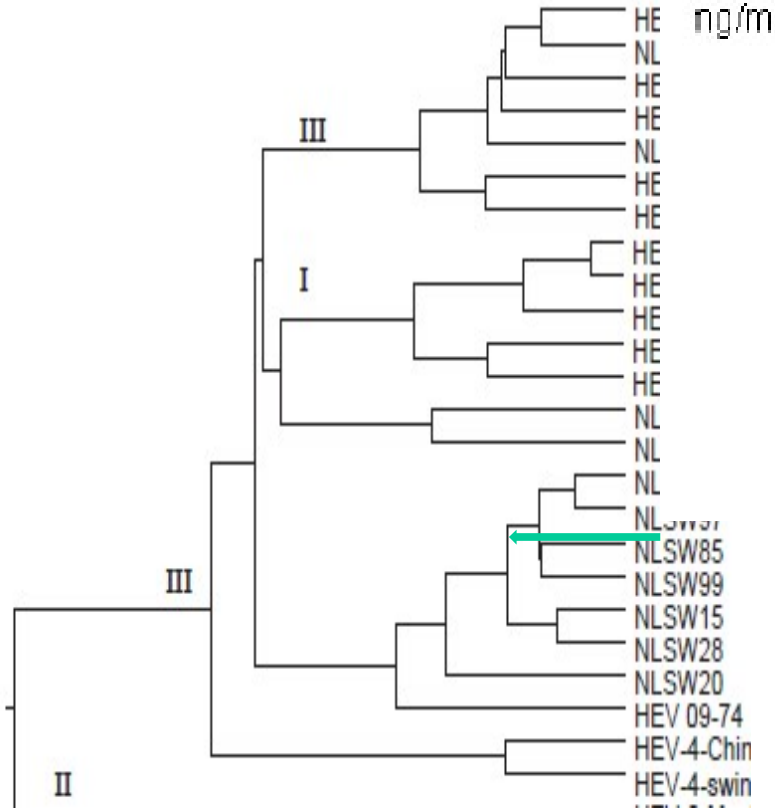
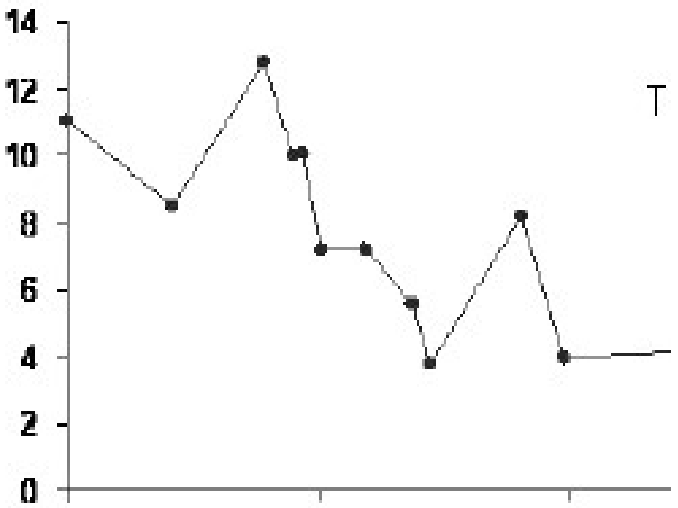
Gastroenterology, Cliniques
Université Catholique de Lou





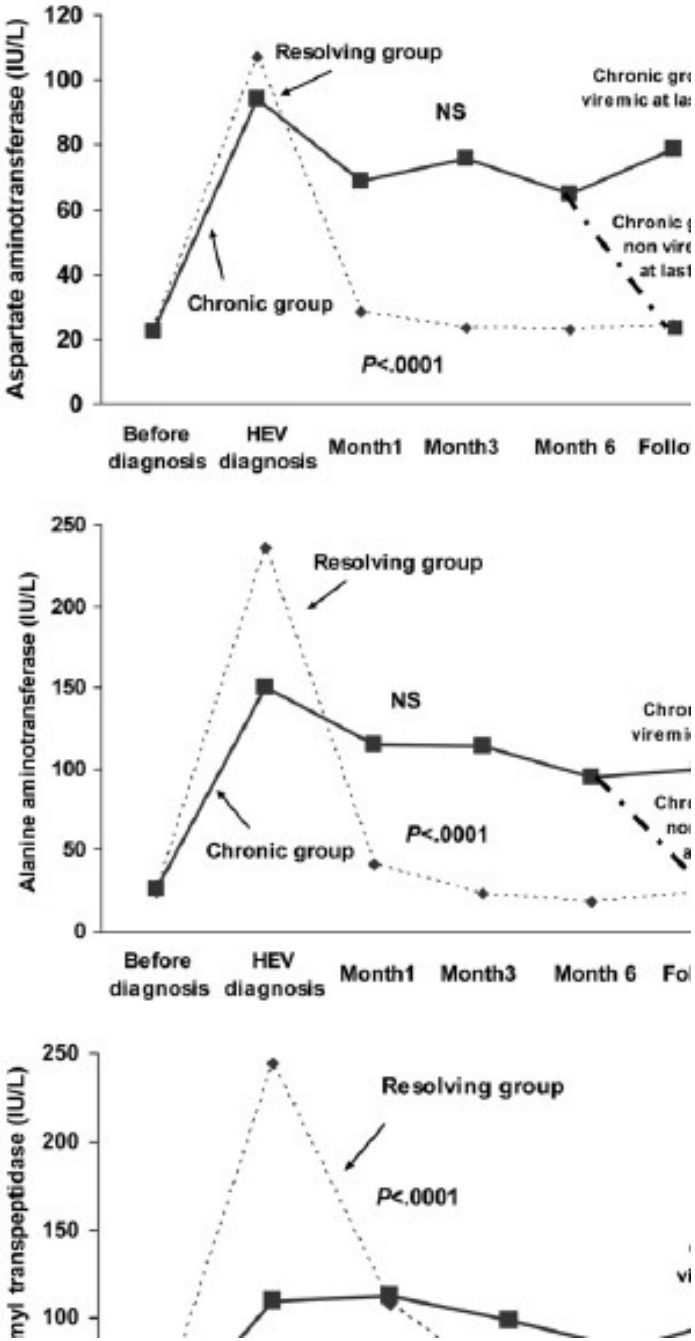


Factors Associated With Chronic Hepatitis in Patients With E Virus Infection Who Have Received Solid Organ Transplar

NASSIM KAMAR,[*,‡,§] CYRIL GARROUSTE,[*,‖] ELIZABETH B. HAAGSMA,[¶] VALÉRIE GARRIGUE,[#] S\
CÉCILE CHAUVET [‡‡], JÉROME DUMORTIER [§§], AMÉLIE CANNESSON [‖‖], ELISABETH CASSUTO-VIC

Table 4. Patient Characteristics at Diagnosis of HEV Infection

Variables	Resolving group (n = 29)	Chronic group (n
Time since transplant (*mo*)	70.3 ± 52.8	41.4 ± 38
Symptoms at presentation (%)	31	32
AST level (*IU/L*)	107 (16–1571)	94 (21–43
ALT level (*IU/L*)	263 (24–2675)	135 (28–87
γ-glutamyl transpeptidase level (*IU/L*)	244 (28–2337)	173 (25–34
Alanine phosphatase level (*IU/L*)	251 (66–1924)	172 (46–77
Bilirubin level (*μmol/L*)	16 (6–75)	7 (5–277
Peak AST level (*IU/L*)	223 (31–1571)	147 (39–87
Peak ALT level (*IU/L*)	272 (29–2675)	167 (32–52
Serum creatinine level (*μmol/L*)	168 ± 69	130 ± 51
Hemoglobin level (*g/dL*)	13.1 ± 1.85	12.9 ± 1.5
White blood cell count (*/mm³*)	7253 ± 2834	6122 ± 23
Lymphocyte count (*/mm³*)	1414 ± 684	1399 ± 70
Platelet count (*/mm³*)	225,655 ± 62,521	190,384 ± 79
Calcineurin inhibitors (%)	75.9	83.9
Cyclosporin A/tacrolimus	9/13	4/43
Cyclosporin A ($mg \cdot kg^{-1} \cdot day^{-1}$)	1.9 ± 0.5	2.24 ± 1.3
Cyclosporin A trough level (*ng/mL*)	88 ± 82	183 ± 10
Cyclosporin A C2 level (*ng/mL*)	543 ± 155	352 ± 24
Tacrolimus ($mg \cdot kg^{-1} \cdot day^{-1}$)	0.06 ± 0.03	0.09 ± 0.0
Tacrolimus trough level (*ng/mL*)	8.7 ± 3.2	10.1 ± 4.3
Belatacept (%)	3.4	0
mTOR inhibitors (%)	24	19.6
Sirolimus trough level (*ng/mL*)	7.8 ± 4.3	8.7 ± 3.0
Everolimus trough level (*ng/mL*)	10.5 ± 7.07	12.1 ± 6.3
Mycophenolic acid (%)	79.3	69.6
Mycophenolic dose ($mg \cdot kg^{-1} \cdot day^{-1}$)	19.2 ± 7.6	20.1 ± 8.0
Azathioprine (%)	0	7.1
Corticosteroids (%)	72.4	69.6



The NEW ENGLAND JOURNAL of MEDICINE

BRIEF REPORT

Hepatitis E Virus and Chronic Hepa

14 cases of acute HEV infection:

- 3 patients receiving liver transplants
- 9 patients receiving kidney transplants
- 2 patients receiving kidney and pancreas transplants.

All patients were positive for serum HEV RNA.

Chronic hepatitis developed in 8 patients:

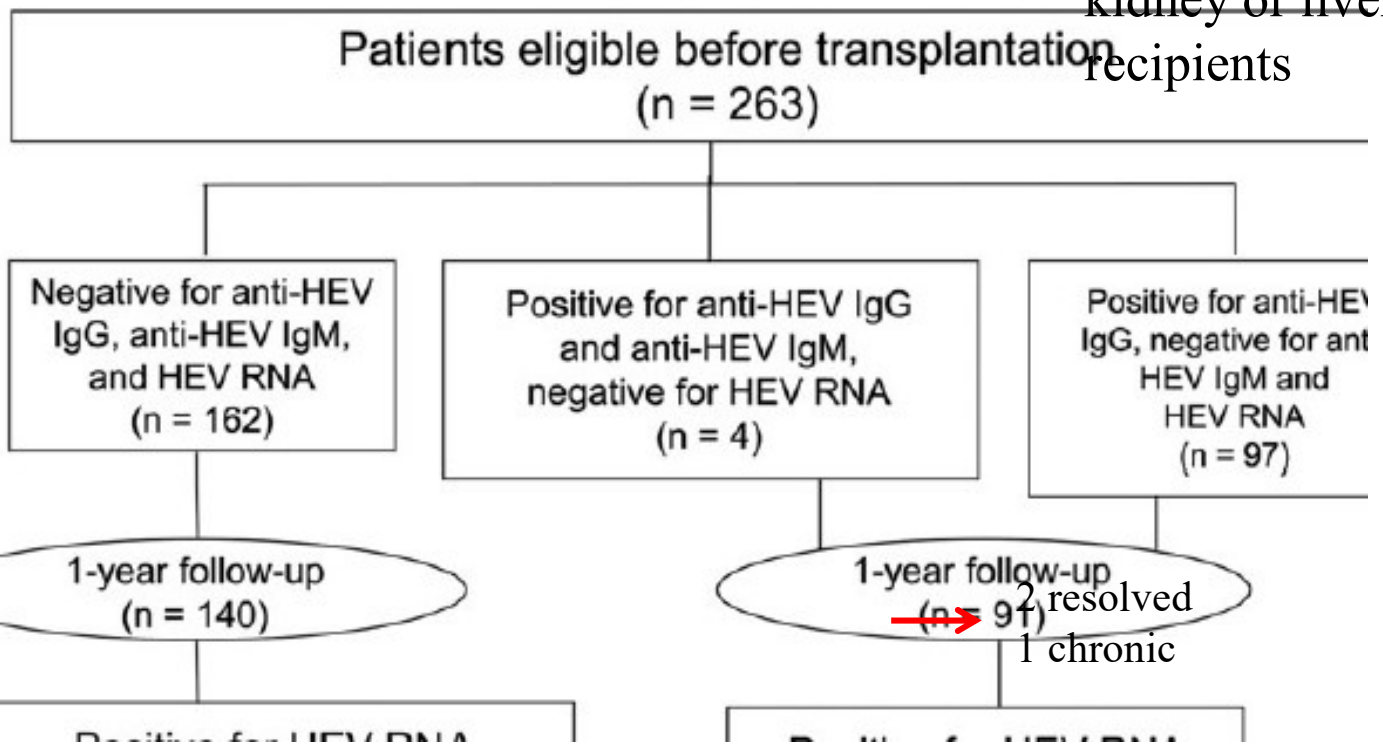
- persistent elevated aminotransferase levels
- serum HEV RNA
- and histologic features of chronic hepatitis.

The time from transplantation to diagnosis was significantly shorter and the total counts of lymphocytes and of **CD2, CD3, and CD4 T** cells were significantly lower in patients in whom chronic disease developed.

Kamar N. et al New Engl J Med 2008

Hepatitis E Virus Reinfections in Solid-Transplant Recipients Can Evolve Into Infections

kidney or liver recipients



1 resolved
2 chronic

2 resolved
1 chronic

Results. A total of 38.4% had anti-HEV IgG at transplantation. The mean concentra IgG at transplantation (8 ± 17.5 U/mL) and 1 year later (6.4 ± 12.0 U/mL, $P = .4$) were sim

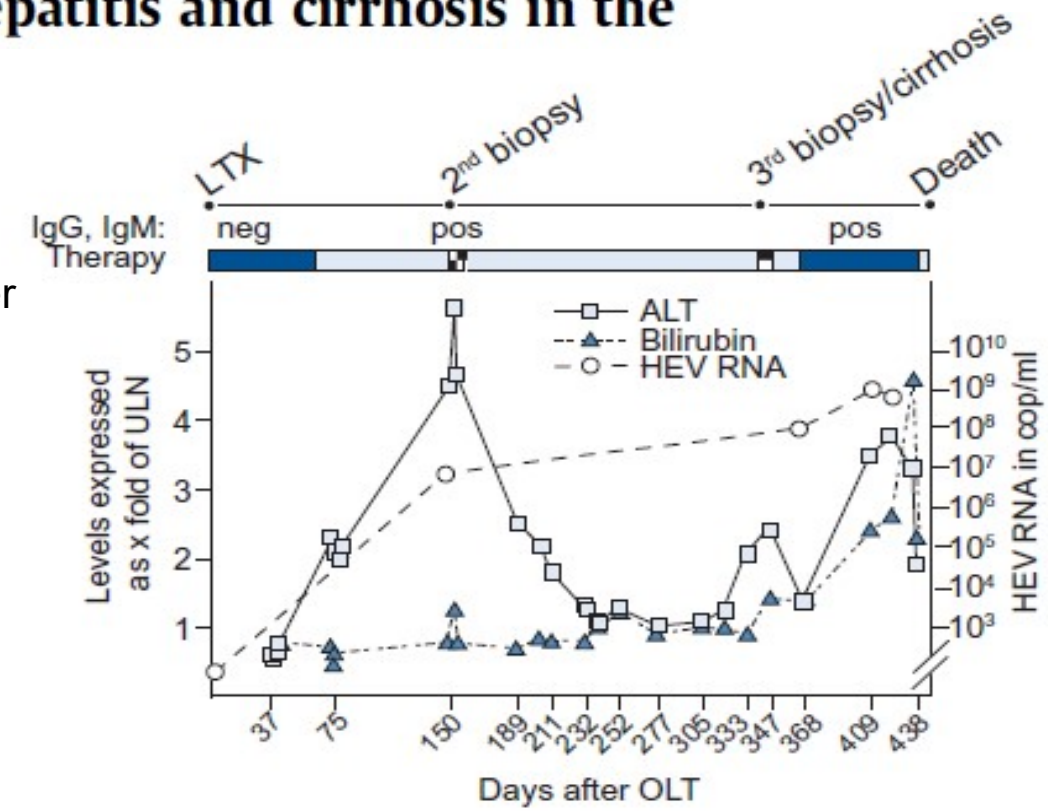
J Hepatol 2012

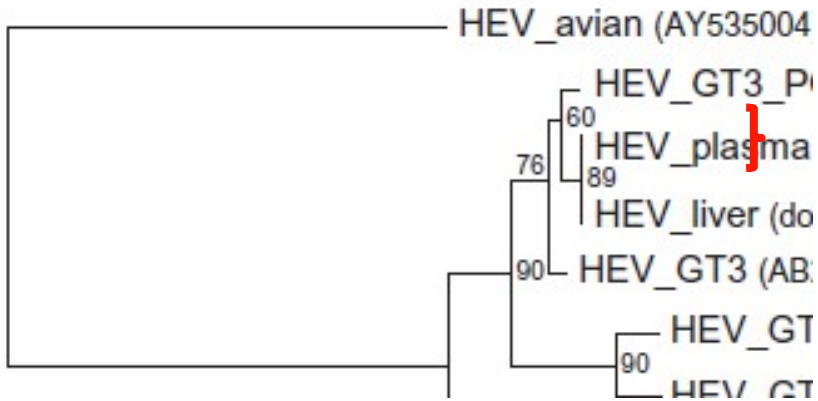
Liver transplant from a donor with occult HEV induced chronic hepatitis and cirrhosis in the

Donor:
- Serum was HEV-Ab and RNA negative
- HEV RNA (high concentration) in liver

Recipient:
- HEV seronegative pre-transplant
- IgG, IgM, PCR pos since 150 days post OLT
- Cirrhosis developed in 15 months
- Died of septic shock

- HEV GT3; identical donor/recipient





Am J Transpl 2010

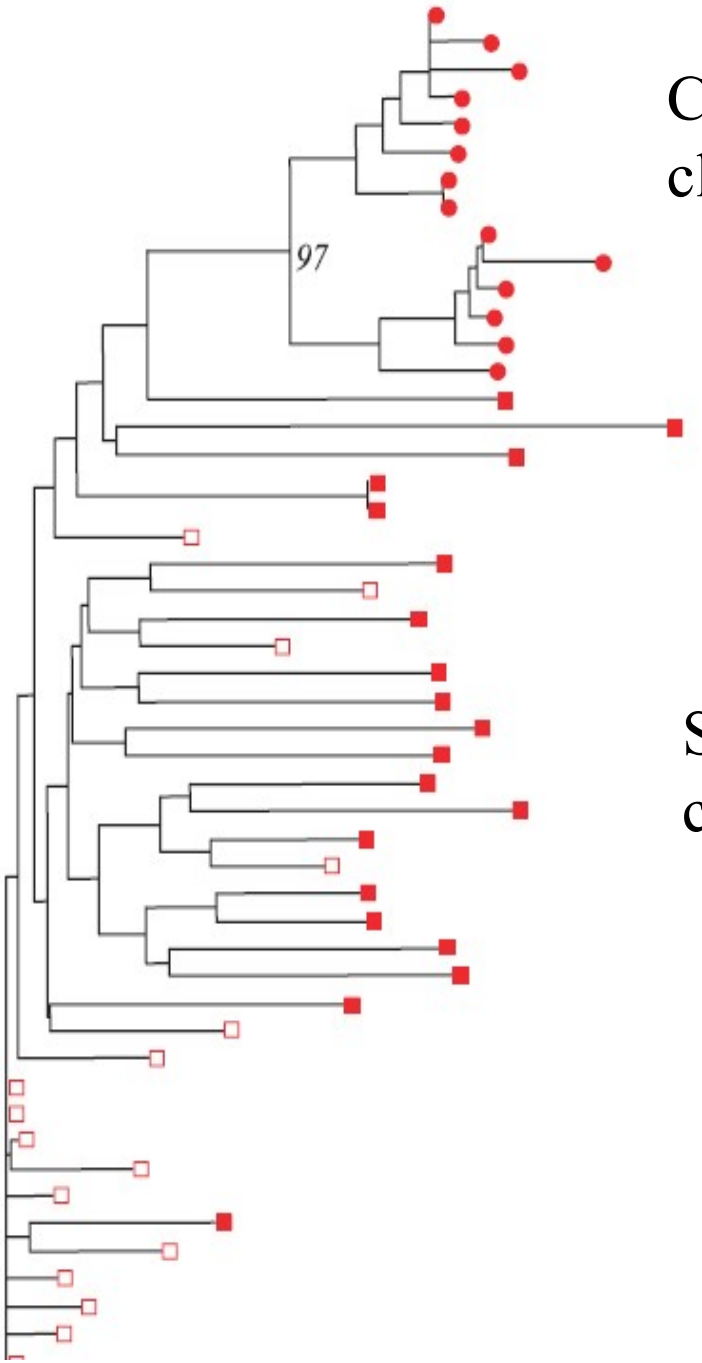
N. Kamar[a,b,*], J. Izopet[c], C. Garrouste[a,d], E. Uro-[c]

Case Report

Hepatitis E Virus-Induced Neurolo
Symptoms in a Kidney-Transplant

CNS disease linked to emergence of neurotropic variant?

- **HEV RNA**
  - **in serum 260 000 cp/mL**
  - **in CSF 1113 cp/mL**
- **Evidence of quasispecies compartmentalization and temporal association :**
  Clonal HEV sequences (ORF1) analyzed in serum and CSF and compared to clonal sequences from serum taken 21 months earlier.



CSF clones

Serum clones

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Diagnostic problems with HEV in transplant setting

Special Section Editors: Peter R. Galle, Peter L.M. Jansen, Fra

Chronic hepatitis E in the immunos

A new source of trouble?

Journal of Hepatology 5

togenic cirrhosis. However, how should the
be made? Diagnostic tools to assess HEV
are available and encompass serological assays
anti-HEV antibodies capable of differentiati
from remote infection (IgG, IgM, IgA). Tl
are generally based on detection of antibodie
the highly conserved and immunogenic capsi
(encoded by the open reading frame 2) and ar
terized by broad activity and good reproc
Highly specific ELISA for quantifying neutrali
bodies to HEV genotypes 1–4 are com
available. Nevertheless, in the reported cases
version occurred on average later than am
immunosuppressed patients (10 months af
infection versus 1–3 weeks in immune c
patients). Even more disturbing is the observa
in three of the 11 patients antibodies remaine
tently negative. Nucleic acid testing, in contra
most sensitive test for ongoing HEV infectio
or real-time PCR may detect viral genomic
serum or stools, especially in acute infection a

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Systematic Serological Testing for Hepatitis E Virus in Ki Transplant Recipients

TABLE 1 Anti-HEV IgG and IgM prevalences in kidney re transplanted for >1 year, according to serological assay us testing

Response by year of testing	No. (%) detected l Adaltis (n = 189)
2012	173
IgG positive	27 (16)
IgM positive	7 (4)
IgM and HEV RNA positive	2 (29)
2013	16
IgG positive	3 (19)
IgM positive	1 (6)
IgM and HEV RNA positive	0 (0)
2014	0
IgG positive	

HEV IgG prevalence was

- 16% with the Adaltis assay (1 March 2012- 27 Jan 2013)
- 42% with the Wantai assay (28 Jan-2013-31 May 2014)

Curr Infect Dis Rep (2016) 18:8
DOI 10.1007/s11908-016-0515-z

Large difference in seroprevalence data according to the assay (2.3 to 43 %); HEV RNA in the serum, ranges from 0 to 3.2 %

Hepatitis E in Transplantation

Table 1 Prevalence and incidence of anti-HEV IgG and HEV RNA in patients with a solid-organ transplant

Study	Number	Organ transplant	Serology tests	Anti-HEV IgG prevalence (%)	HEV RN prevalenc
Abravanel et al. [72]	700	KT/LT/SPK	Adaltis	12.7	–
Abravanel et al. [73]	263	KT/LT	Wantai	38.4	–
Buffaz et al. [74]	206	LT	Wantai	29	–
Buti et al. [75]	108	KT/LT	Biokits	2.3	–
Haasgsma et al. [76]	285	LT	Genelabs	3.5	1.75
Koning et al. [77]	145	LT	Wantai	42	0
Laverdure et al. [78]	96	LT	Wantai	8.3	–
Moal et al. [79]	1350	KT	–	–	1.2
Moal et al. [80]	578	KT	Wantai	43	–
Magnusson et al. [81]	62	Lung T	Mikrogen	13	0
Naik et al. [82]	205	KT	Wantai	20.5	0
Pas et al. [83]	1200	SOT	Wantai	–	1
Pischke et al. [84]	226	LT	Abbot	4.4	0.9
Pischke et al. [85]	274	HT	Genelabs	11.3	1.5
Pischke et al. [86]	95	Lung T	MP	5.3	3.2

Outline

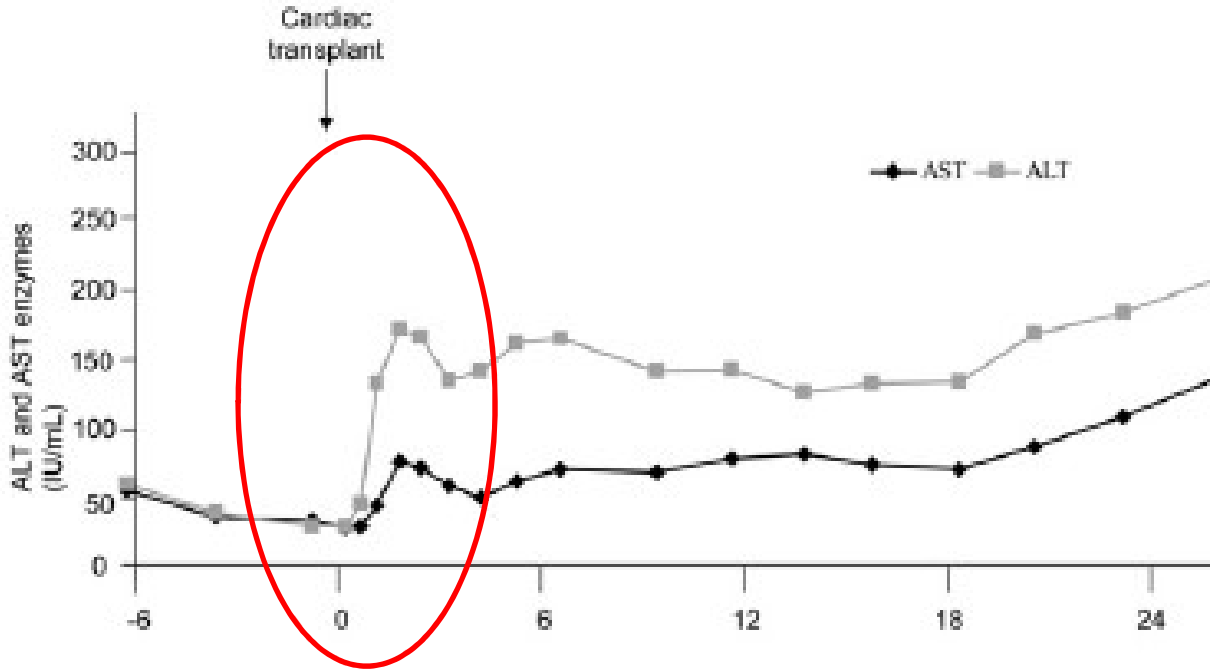
- Introduction to HEV
- Contexts of HEV acquisition in transplant
- Impact of immune suppression on clinical evolution
- How to study HEV prevalence/incidence
- Clinical management (therapeutic options)

•Post-transplant HE misdiagnosed as drug-induced liver inlury

Chaillon A. J Heart Lung Transplant. 2011 Jul;30(7):841-3

Sustained virologic response with ribavirin in c

Ribavirin may induce a sustained virologic response in heart transplant patients with chronic HEV infection



- 3-month course of oral ribavirin (17 mg/kg/day)
- Serum HEV RNA undetectable after 1 month of Tx;
- Liver function indicators returned to normal reference ranges.
- The main ribavirin-induced side effect was a significant but well-tolerated anemia.

N ENGL J MED 370;12 NEJM.ORG MARCH 20, 2014 MEDICINE

ORIGINAL ARTICLE

Ribavirin for Chronic Hepatitis E Virus Infection in Transplant Recipients

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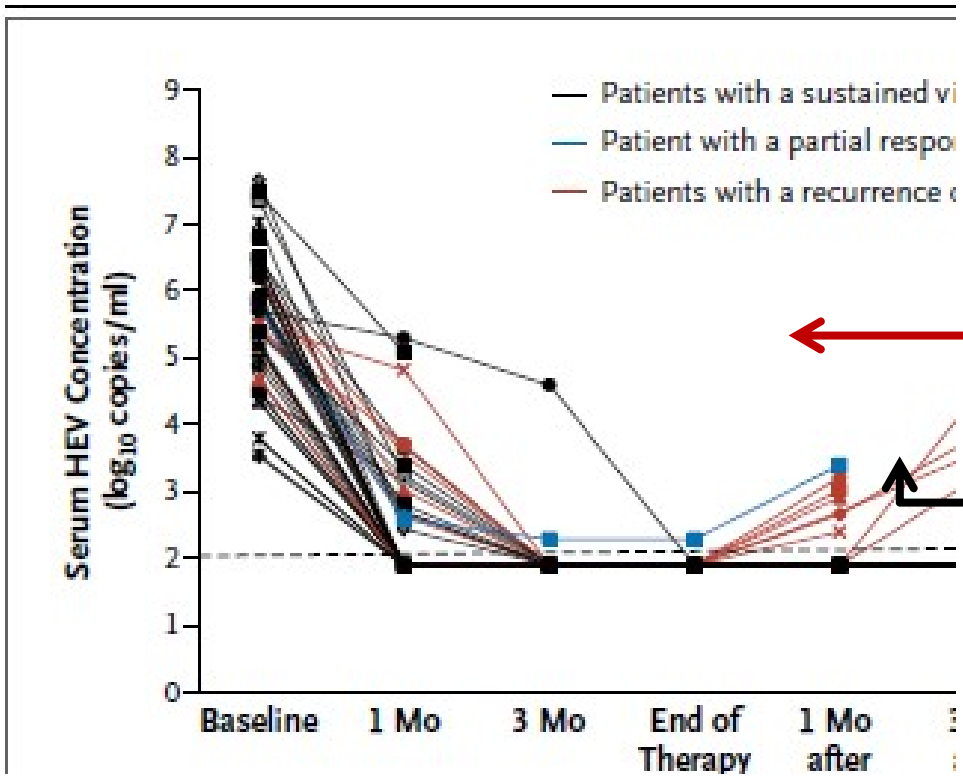
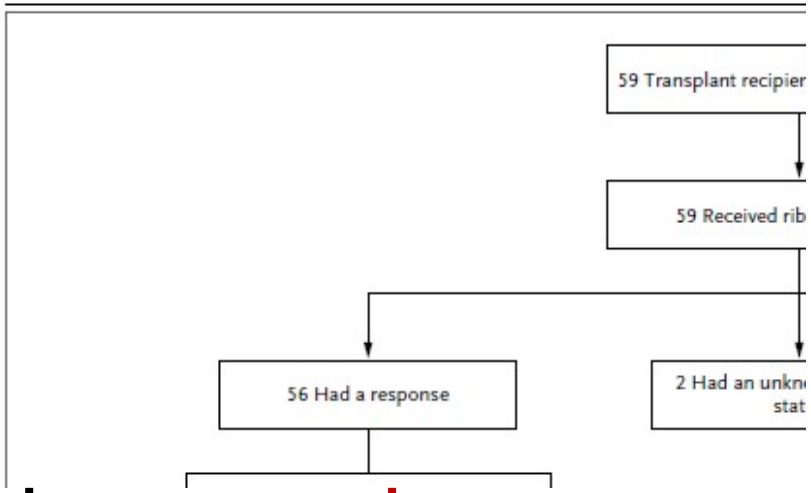


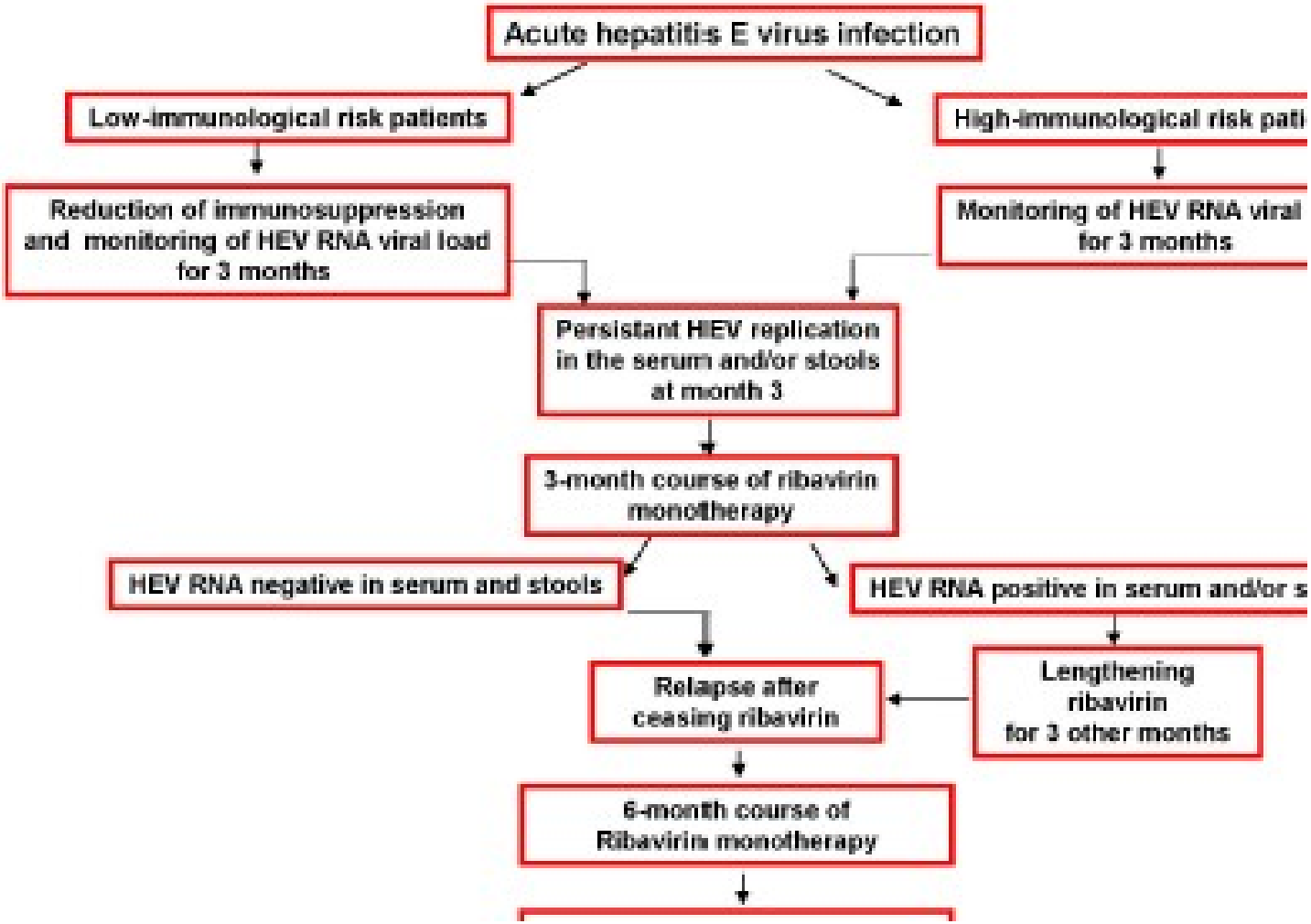


viruses

Viruses 2016, 8, 222; doi:10.3390/v8

Review

Treatment of HEV Infection in Patients with a Solid-Organ Transplant and Chronic Hepat



What are the lessons?

- HEV is an emerging pathogen whose impact in the transplant setting is increasingly recognized
- Different contexts of HEV acquisition
- Gen 3 almost exclusively involved
- Chronic evolution major problem (immune suppression major driver)
- Diagnostic issues (discrepant serological tests), also affecting retrospective studies
- Therapeutic options available but sperimental

Grazie

A Daniele Lapa, Anna Rosa Garbuglia
A tutti voi