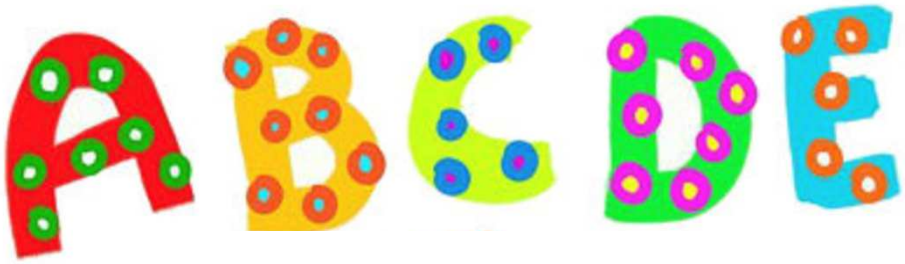


JORNADAS 2018
DE ACTUALIZACIÓN
EN ATENCIÓN FARMACÉUTICA
AL PACIENTE
CON PATOLOGÍAS VÍRICAS
Madrid, 10-11 de mayo de 2018

Otras hepatitis no B no C

Juan Berenguer
Hospital General Universitario Gregorio Marañón (IiSGM)
Madrid

SaludMadrid Hospital General Universitario Gregorio Marañón

IiSGM

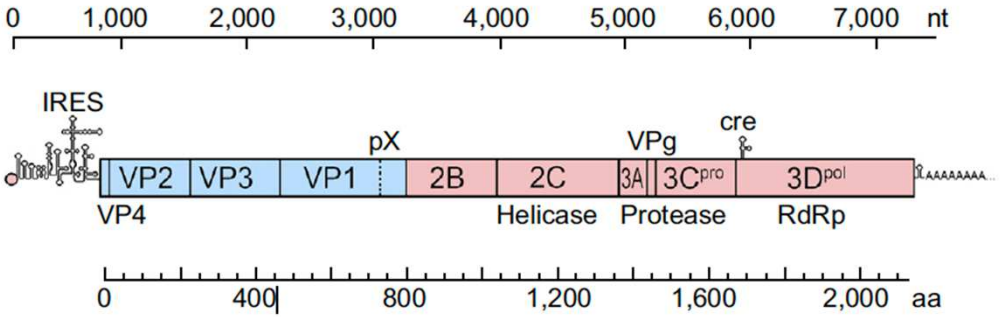
Caso clínico

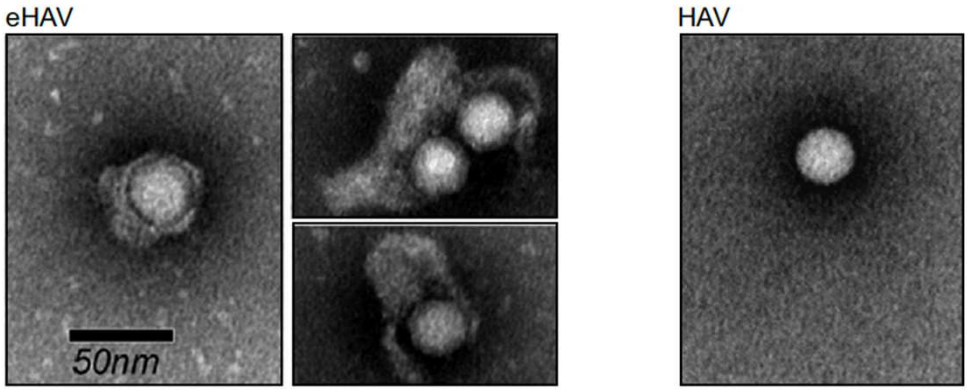
- ♂ 25 a HSH (Europa del Este)
- Mayo 2017: HIV + (MAP)
- Evaluación inicial
  - CD4+ 586/mm3, CV VIH 5,652 copias/mL
  - ALT 20, AST 17
  - VHA -, HBsAg-, HBcAc-, HCV-, VDRL-
- Junio 13, 2017
  - Astenia e ictericia de aparición súbita
  - Hepatomegalia dolorosa
  - ALT 2.571 U/L, AST 1.005 U/L, BR 6,70 mg/dL, FA 84 U/L, GGT 130 U/L

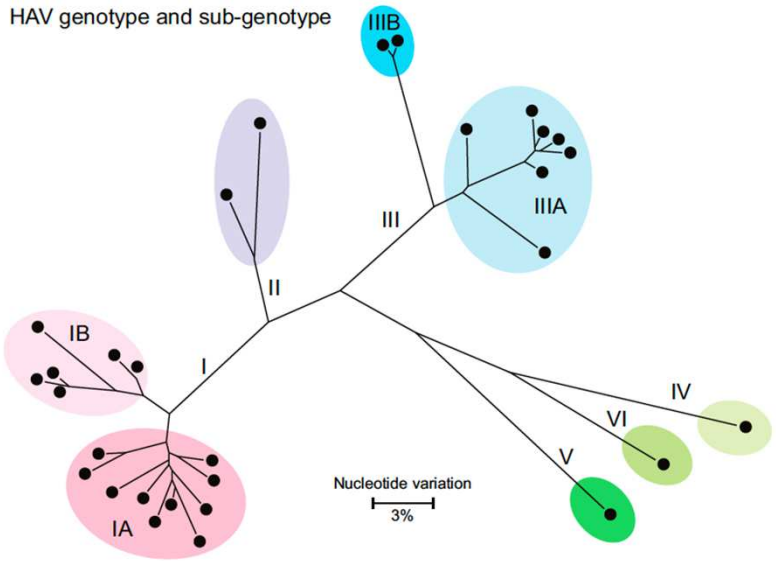
¿Diagnóstico más probable?

1. Hepatitis luética
2. Hepatitis C aguda
3. Hepatitis A aguda
4. Hepatitis B aguda

Hepatitis A Virus







Typical manifestations

The incubation period of HAV averages 28 days (range 15 to 50 days)

Clinical	• Most adults with HAV infection have symptomatic illness • Abrupt onset of nausea, anorexia, fever, malaise, and abdominal pain. • This is followed by choluria / acholia and then by jaundice and pruritus.
Laboratory	• ↑ALT/AST (>1000 IU/dL), followed by ↑ of bilirubin (up to 10 mg/dL). • ALT/AST peak approximately 1 mo. after exposure and then decline. • The serum bilirubin concentration usually declines within 2 wks of peak levels.

- Fulminant hepatic failure < 1% of cases (Age >50 and other liver diseases)
- Recovery within 2-3 mo in 85 %. Complete recovery is observed by 6 mo.
- Contagious during the incubation period and remain so for about a week after jaundice appears.

Diagnosis

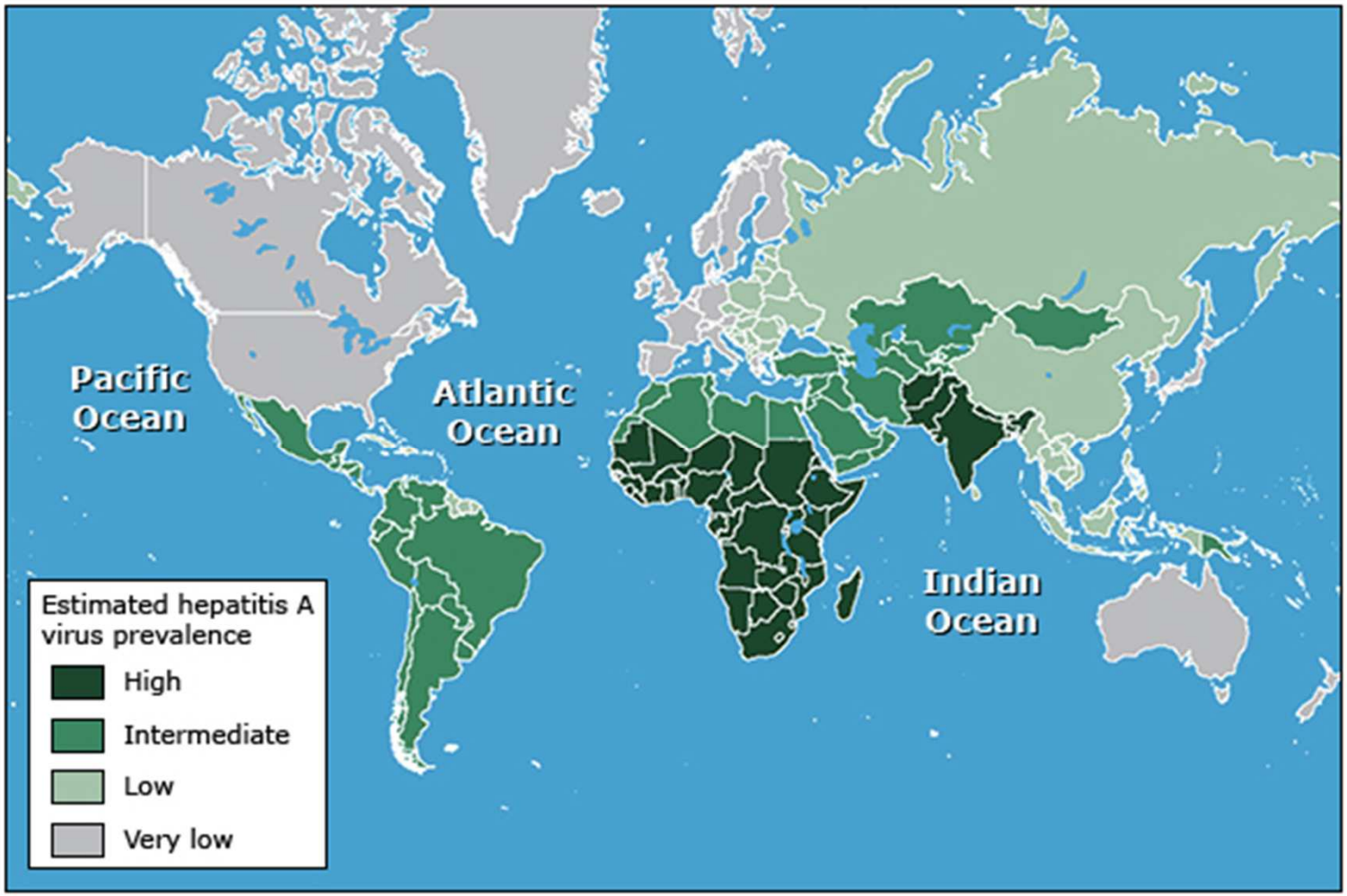
- **Detection of serum IgM anti-HAV antibodies**
  - Detectable at the time of symptom onset and remain detectable for 3-6 mo.
  - Persistent among patients with relapsing hepatitis
  - Detection of serum IgM antibodies in the absence of clinical symptoms
    - Prior hepatitis A infection with prolonged persistence of IgM
    - False-positive result
    - Asymptomatic infection (more common in children <6 years of age).
- **Detection of serum IgG anti-HAV antibodies**
  - Appear early in the convalescent phase of the disease
  - Remain detectable for decades, and are associated with lifelong protective immunity.
  - Detection of anti-HAV IgG in the absence of anti-HAV IgM
    - Past infection
    - Vaccination

Modes of hepatitis A virus transmission*

- **Person-to-person contact**
  - Transmission within households
  - Sexual transmission
  - Residential institution transmission
  - Daycare center transmission
  - Transmission among military personnel
- **Contact with contaminated food or water**
  - Consumption of raw or undercooked shellfish, vegetables, or other foods
  - Consumption of foods contaminated by infected food handlers
- **Blood transfusion**
- **Illicit drug use**

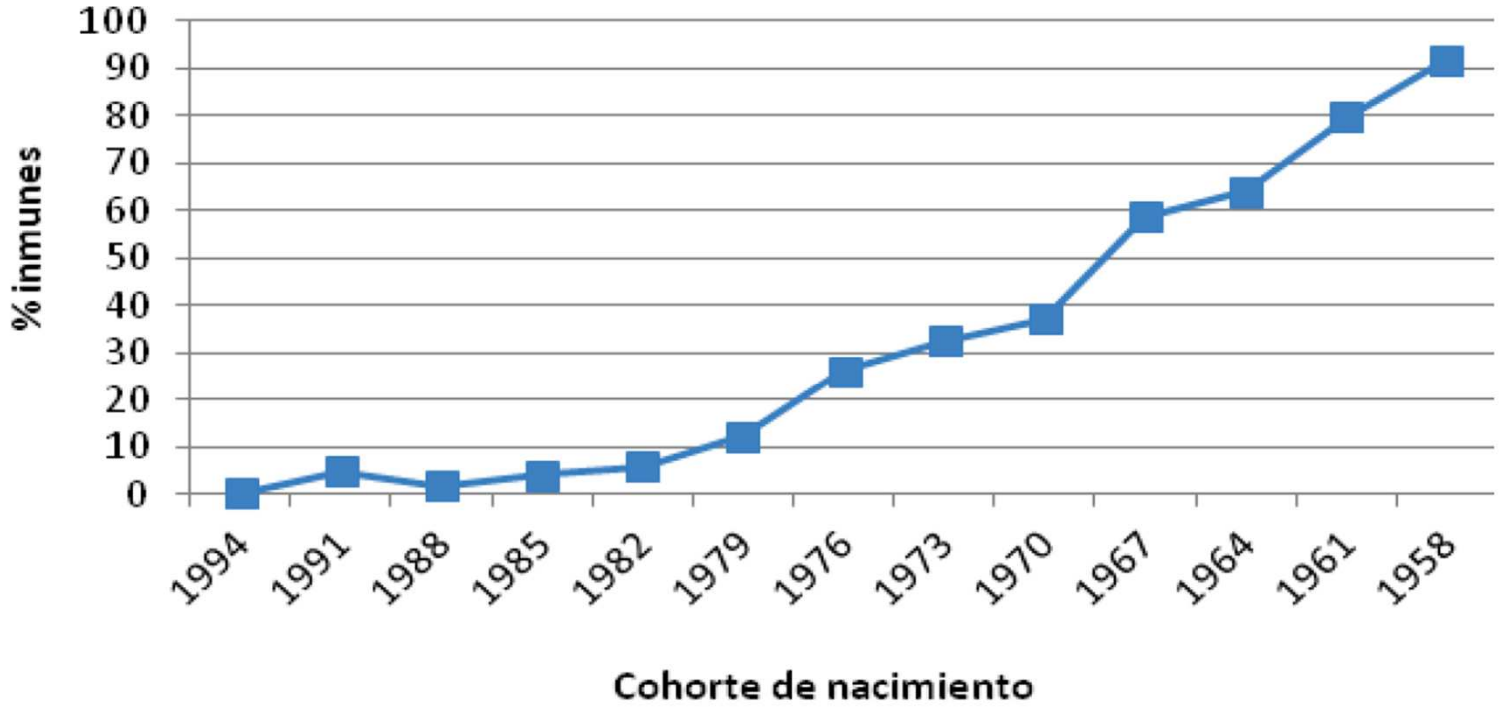
*HAV virus is usually transmitted via the fecal-oral route

Prevalence of antibodies against HAV



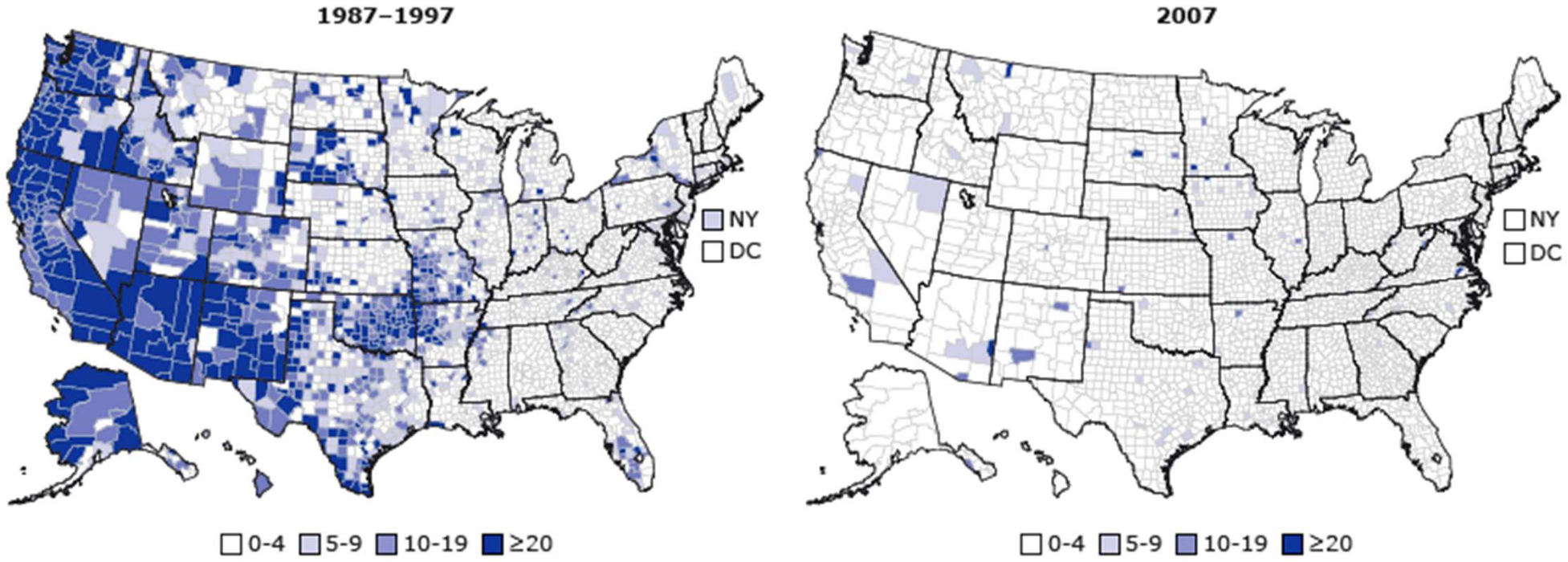
Jacobsen KH, et al. Vaccine 2010; 28:6653.

Porcentaje de población inmune a hepatitis A, por cohorte de nacimiento



Fuente: Estudio seroepidemiológico en España, 1996. CNE. ISCIII[26]

Incidence of reported acute hepatitis A cases United States, 1987 to 1997 (pre-vaccine) and 2007



Murphy TV, et al. MMWR Suppl 2016; 65:29.

VIDA SANA

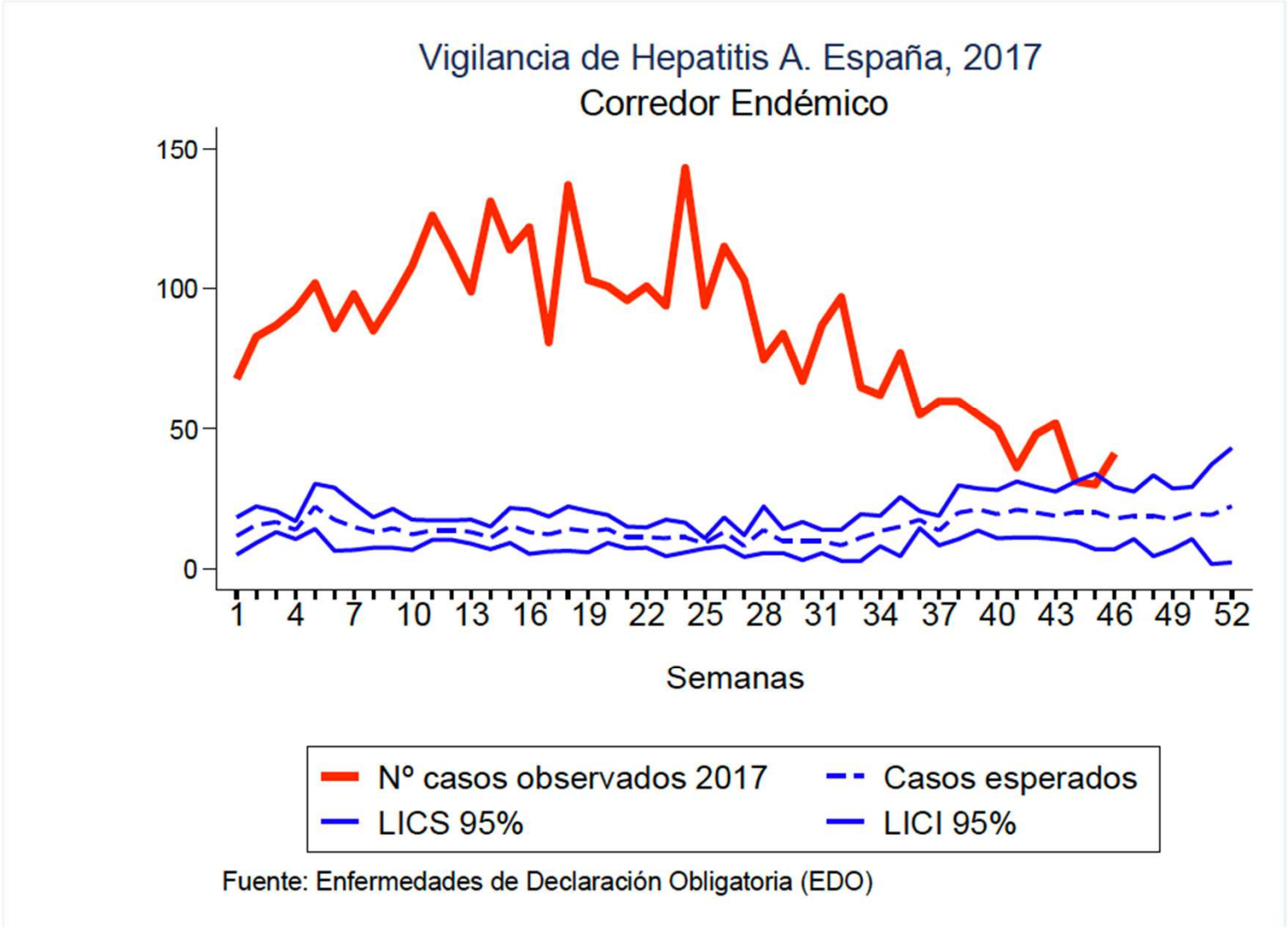
España vive el mayor brote de hepatitis A desde los noventa, cuando llegó la vacuna

■ Los médicos de familia muestran tranquilidad, pero sí alertan de la relajación en los métodos de control de las enfermedades de transmisión sexual

Publicado el 04/09/2017 | Actualizado el 31/01/18 - 11: 59

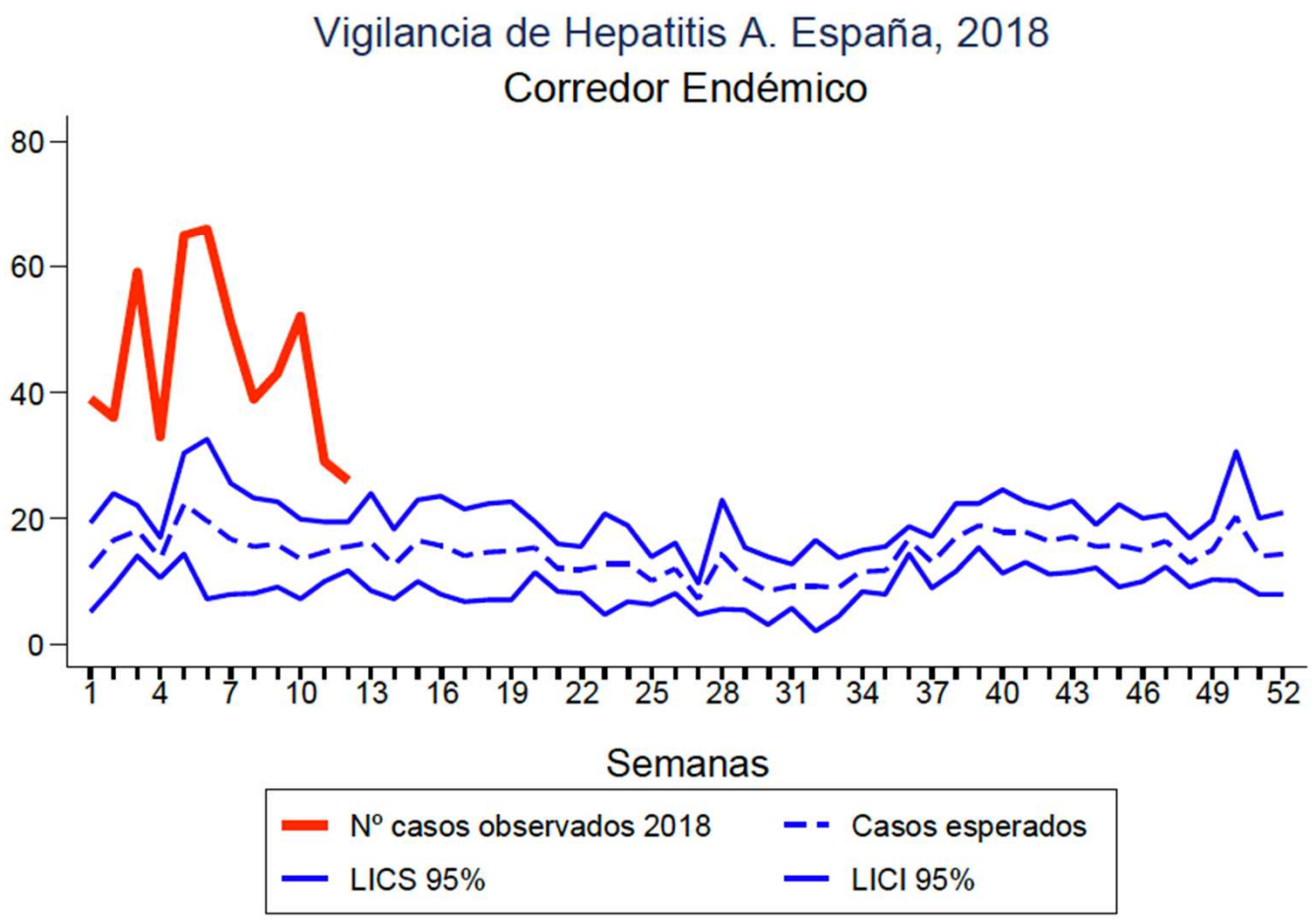
CRISTINA CASTRO cristina.castro@elindependiente.com @criscastro_sm

Figura 1. Corredor Endémico de Hepatitis A. Semanas epidemiológicas desde la 1 hasta la 46 de 2017



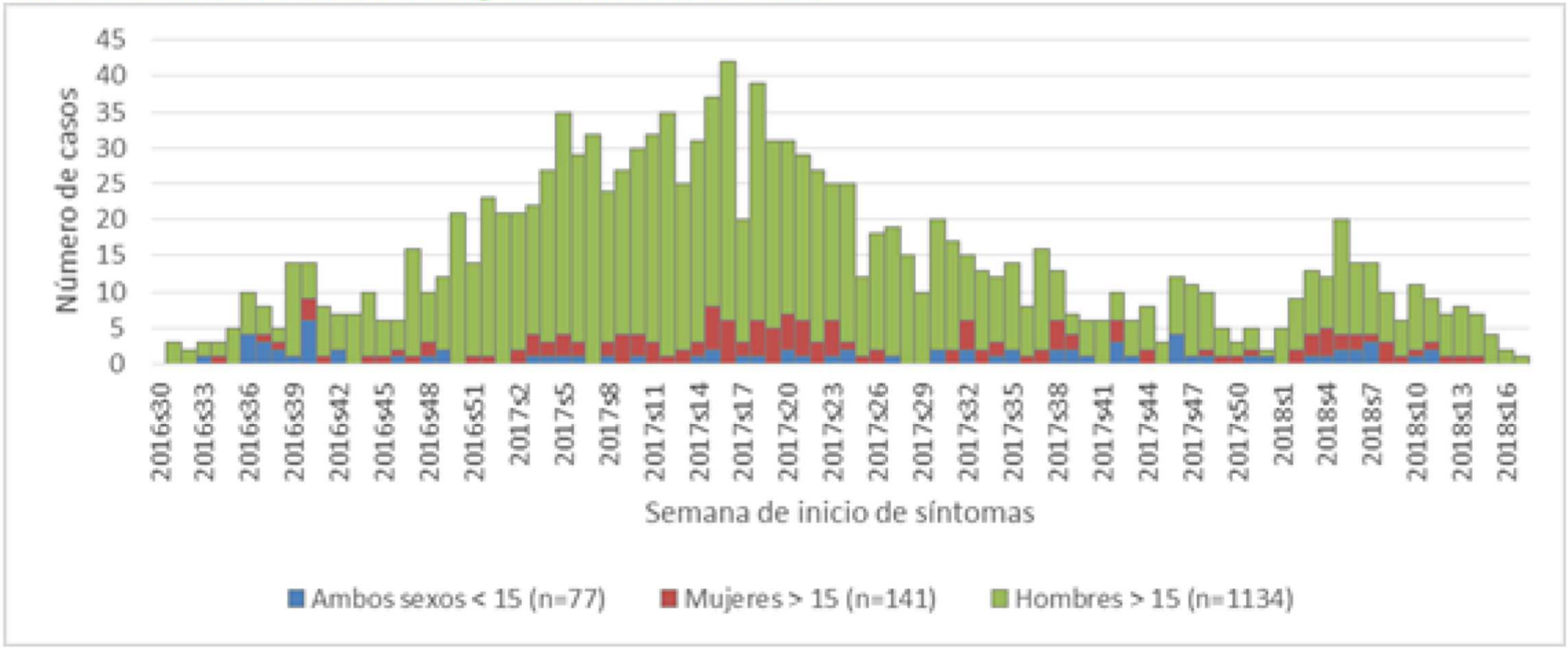
Fuente: Enfermedades de Declaración Obligatoria (EDO)

Figura 1. Corredor Endémico de Hepatitis A. Semana epidemiológica 12 de 2018*



Fuente: Enfermedades de Declaración Obligatoria (EDO)

Casos de hepatitis A por sexo, edad y semana de inicio de síntomas. Comunidad de Madrid. Sistema de Vigilancia de Enfermedades de Declaración Obligatoria. Años 2016 a 2018*



Prevention of HAV infection

- **Protection prior to exposure**
  - Vaccination
  - Immune globulin
  - Attention to hygienic practices

- **Protection following exposure**
  - Immune globulin
  - Vaccination

Vacunas (e IGIV) frente a VHA en España

- GSK (Havrix 1440 para adulto y Havrix 720 para personas entre 1 y 18 años)
- MSD (Vaqta 50 para adultos y Vaqta 25 para personas entre 1 y 17 años)

- GSK (Twinrix pediátrica y adulto) con antígenos frente a VHA y VHB

- BEHRING S.A (Beriglobina P de CSL. mínimo de 100 UI de Ac anti VHA en 1ml)
  - Única inmunoglobulina humana inespecífica autorizada y comercializada para la profilaxis pre o pos exposición de hepatitis A

Consejo Interterritorial
SISTEMA NACIONAL DE SALUD

PROBLEMAS DE SUMINISTRO DE VACUNAS FRENTE A HEPATITIS A. RECOMENDACIONES.

Recomendaciones acordadas en reunión de Comisión de Salud Pública, 10 de mayo de 2017.

4. RECOMENDACIONES DE UTILIZACIÓN DE LAS DOSIS DISPONIBLES EN LA SITUACIÓN ACTUAL

1. En la situación actual de problemas de suministro de vacunas, se vacunará exclusivamente a las personas que pertenecen a los grupos de riesgo especificados en el documento "Recomendaciones de vacunación frente a hepatitis A en grupos de riesgo", disponible en la página web del Ministerio de Sanidad, Servicios Sociales e Igualdad (MSSSI) a través del siguiente enlace: http://msssi.es/profesionales/saludPublica/prevPromocion/vacunaciones/docs/Recomend_HepatitisA.pdf

   Siempre que sea posible, se realizará serología (determinación de IgG) para determinar la susceptibilidad en nacidos antes de 1977*. Se estima que esta medida permitirá un ahorro de alrededor de un 30% de dosis de vacuna.

Recomendaciones de Utilización de Vacuna Frente a VHA en Adultos (CISNS)

- No se recomienda la vacunación sistemática
  - Cataluña, Ceuta y Melilla incluyen la vacunación sistemática en niños

- Se recomienda la vacunación frente a HA en grupos de riesgo

- Para determinar la susceptibilidad de las personas nacidas antes de 1977* incluidas en grupos de riesgo, se realizará serología (VHA IgG) siempre que sea posible.

Grupos de riesgo según el CISNS - 2013

- Viajeros a zonas de alta o moderada endemicidad
- Hepatopatía crónica incluyendo VHC y VHB
- Pacientes hemofílicos que reciben hemoderivados
- Trasplantados o candidatos a trasplante
- Infectados por el VIH
- Personas con estilos de vida que conllevan un mayor riesgo de infección: HSH y UDI
- Familiares o cuidadores que tengan contacto directo con pacientes con hepatitis A
- Sujetos con mayor riesgo ocupacional (categoría muy amplia)
- Manipuladores de alimentos
- Personal que trabaja en guarderías.

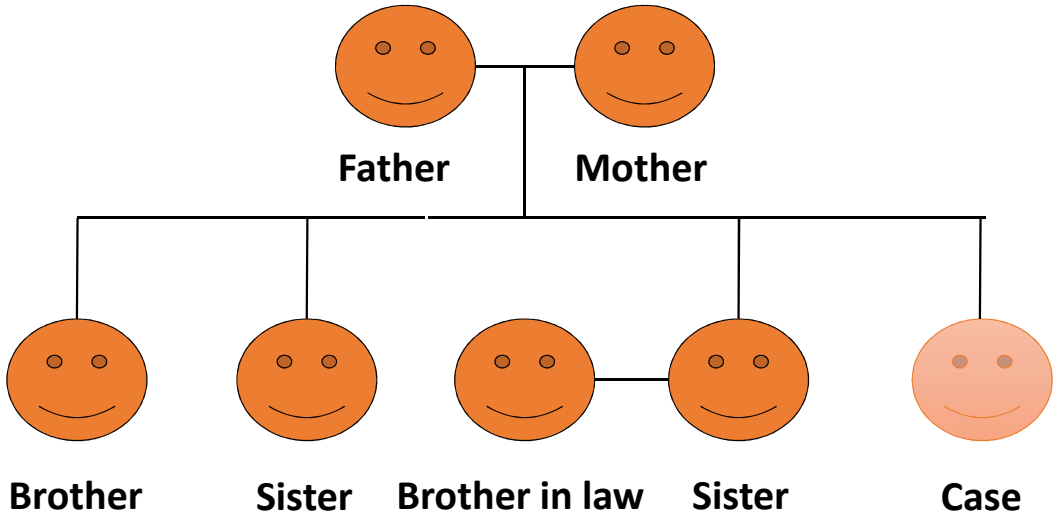
MINISTERIO DE ECONOMÍA Y COMPETITIVIDAD
Instituto de Salud Carlos III
MINISTERIO DE SANIDAD, SERVICIOS SOCIALES E IGUALDAD
Red Nacional de Vigilancia Epidemiológica

Caso

- Hombre de 32 años
- Vive en un pueblo de Córdoba
- Consulta al medico por diarrea, vómitos y malestar general
- AST 650 IU/dL and ALT 750 IU/dL
- Pruebas negativas: IgM VHA, HBsAg, VHC (EIA y ARN), EBV, CMV
- **RT-PCR VHE: 223.517 IU/mL**
- ¿Ha consumido carne de jabalí?
  - “Si, mi padre y mi hermano son cazadores. Hace unas semanas cazaron uno en Almodóvar del Río.”

Rivero-Juarez et al Zoonoses Pub Health 2017

Cribado familiar Hepatitis E



Rivero-Juarez et al Zoonoses Pub Health 2017

Filiación del caso

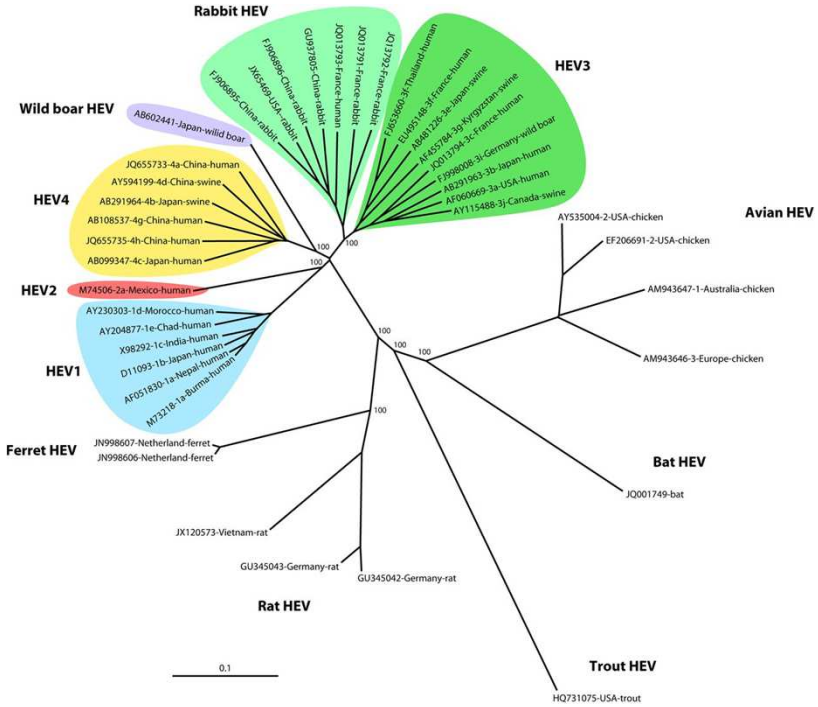
230.500 copias/gr

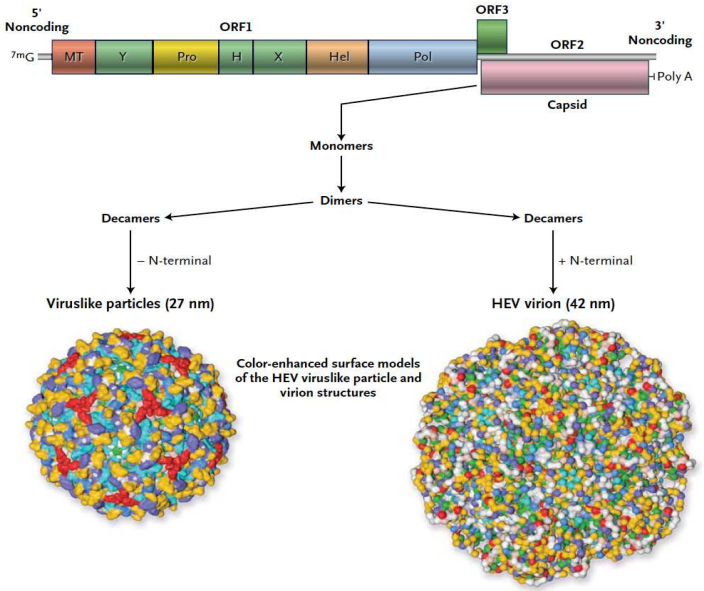
155.300 copias/gr

Rivero-Juarez et al Zoonoses Pub Health 2017

Hepatitis E Virus (HEV)

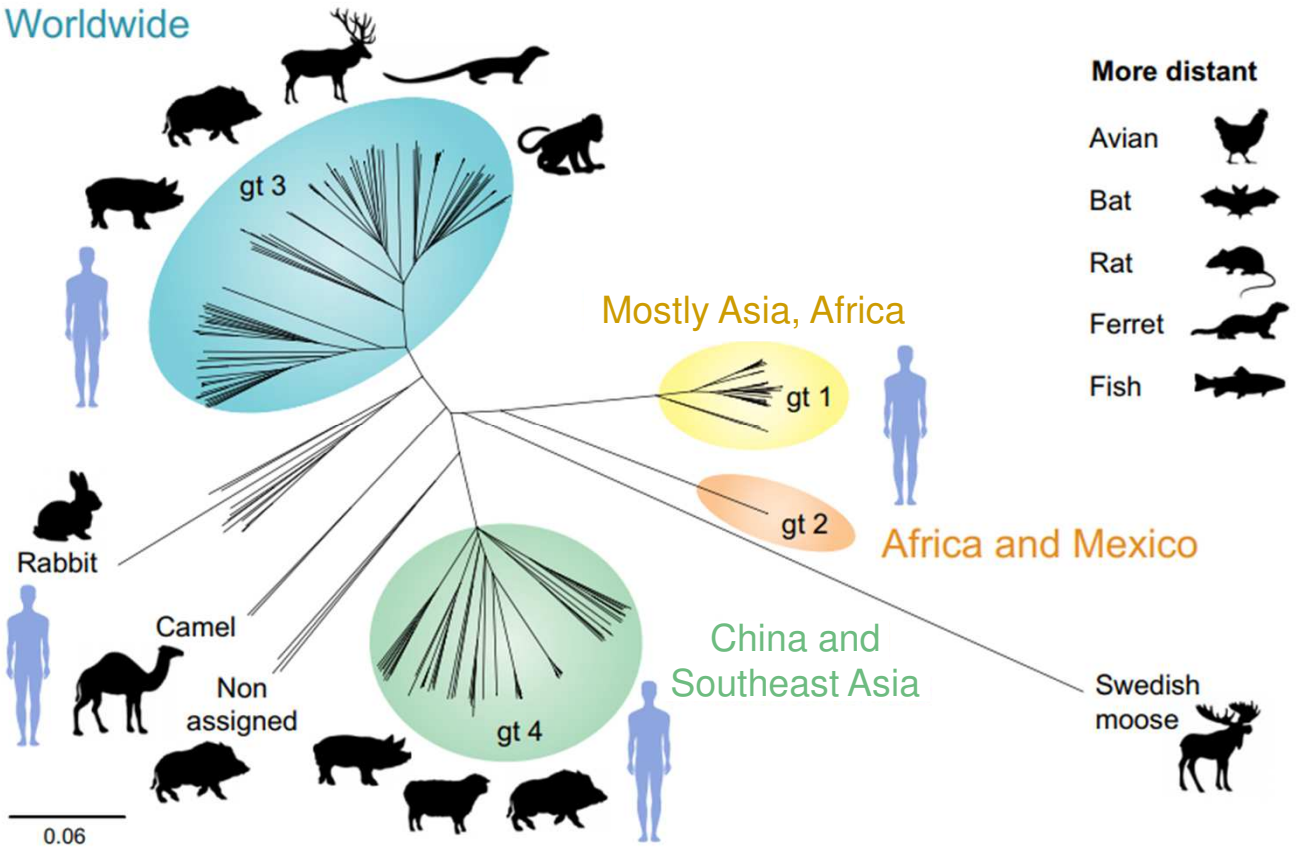
- *Orthohepeviridae* family[1]
- RNA+ non-enveloped: 7,2 kba[2]
- Four know genotypes that can infect humans[3]





1. Hepeviridae Study Group. J Gen Virol 2014
2. Hoofnagle. NEJM 2012
3. Kamar. Clin Microb Infect 2014

Phylogenetic relationship of hepeviruses identified in various hosts



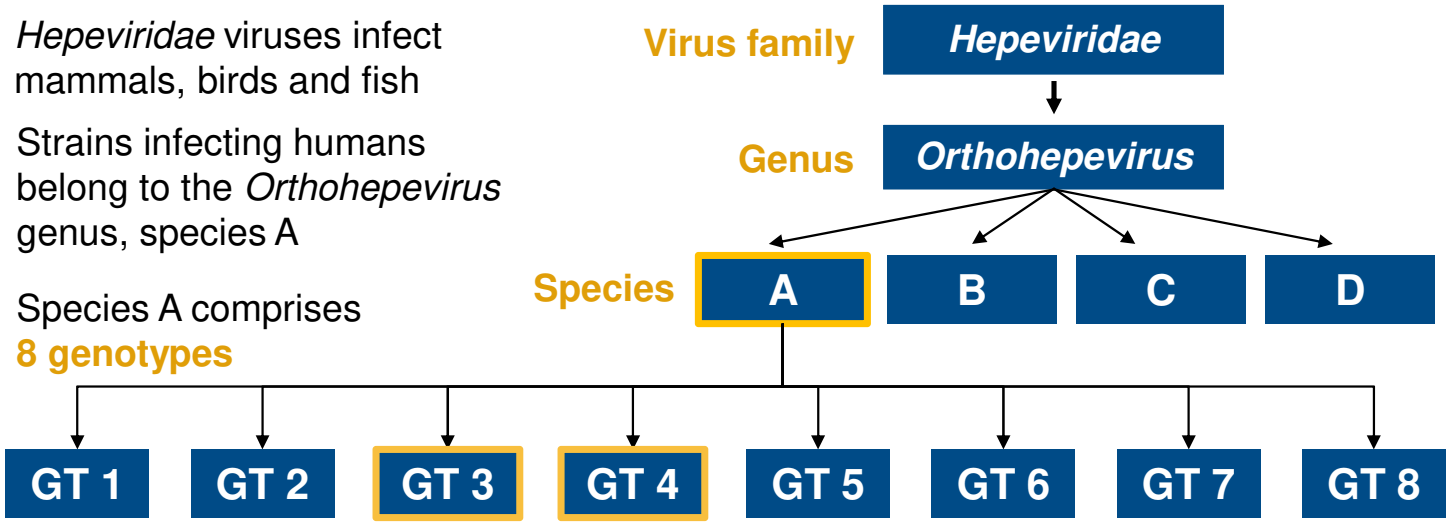
Debing Y, et al. J Hepatol 2016;65:200–12

Virology of HEV

Hepeviridae viruses infect mammals, birds and fish

Strains infecting humans belong to the *Orthohepevirus* genus, species A

Species A comprises **8 genotypes**



- Only infect humans
- **Faecal–oral spread** via contaminated water
- Large **outbreaks**
- Brief, **self-limiting**
- Never chronic
- High mortality in **pregnancy** (25%)

- **Endemic** in animal species; eg, pigs and wild boar
- **Zoonotic** infections in humans
- **High-income countries**
- China: GT 4 most common
- S. America: GT 3 only

- Have only been reported in wild boar

- GT 7 identified in patient regularly consuming camel meat and milk
- Have since been identified in camels

Focus of this CPG

EASL The Home of Hepatology

EASL CPG HEV. J Hepatol 2018;doi: 10.1016/j.jhep.2018.03.005 [Epub ahead of print]

Hepatitis E Virus Genotype 3 in Shellfish, United Kingdom

Presence of hepatitis E RNA in mussels used as bio-monitors of viral marine pollution

Domenica Donia[a,*], Maria Chiara Dell'Amico[b], Anna Rita Petrinca[a], Ilaria Martinucci[b], Maurizio Mazzei[b], Francesco Tolari[b], Maurizio Divizia[a]

[a] Department of Public Health, Faculty of Medicine, University of Rome Tor Vergata, Rome, Italy
[b] Department of Animal Pathology, University of Pisa, Pisa, Italy

Journal of Viral Hepatitis, 2015 doi:10.1111/jvh.12406

Experimental infection of pregnant rabbits with hepatitis E virus demonstrating high mortality and vertical transmission

J. Xia, L. Liu, L. Wang, Y. Zhang, H. Zeng, P. Liu, Q. Zou, L. Wang and H. Zhuang *Department of Microbiology and Infectious Disease Center, School of Basic Medical Sciences, Peking University Health Science Center, Beijing, China*

Received November 2014; accepted for publication February 2015

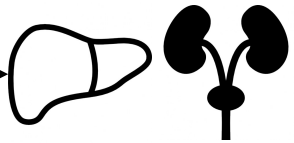
Hepatitis E virus in blood components: a prevalence and transmission study in southeast England

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

Annals of Internal Medicine

OBSERVATIONS

Transmission of Hepatitis E Virus by Plasma Exchange: A Case Report

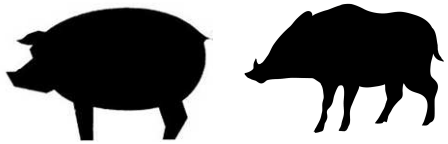


Case Report

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

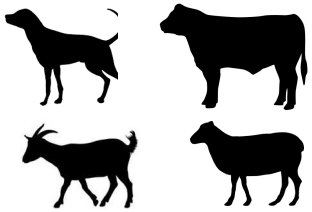
Liver transplant from a donor with occult HEV infection induced chronic hepatitis and cirrhosis in the recipient

B. Schlosser[1], A. Stein[2], R. Neuhaus[3], S. Pahl[4], B. Ramez[1], D.H. Krüger[2], T. Berg[1,5,*,†], J. Hofmann[2,†]



High Proportion of Asymptomatic Infections in an Outbreak of Hepatitis E Associated With a Spit-Roasted Piglet, France, 2013

Yvonnick Guillois,[1] Florence Abravanel,[2] Takayuki Miura,[3] Nicole Pavio,[4] Véronique Vaillant,[5] Sébastien Lhomme,[2] Françoise S. Le Guyader,[3] Nicolas Rose,[6] Jean-Claude Le Saux,[3] Lisa A. King,[1] Jacques Izopet,[2] and Elisabeth Couturier[5]



CLINICAL AND EXPERIMENTAL VACCINE RESEARCH

Hepatitis E virus infections in humans and animals

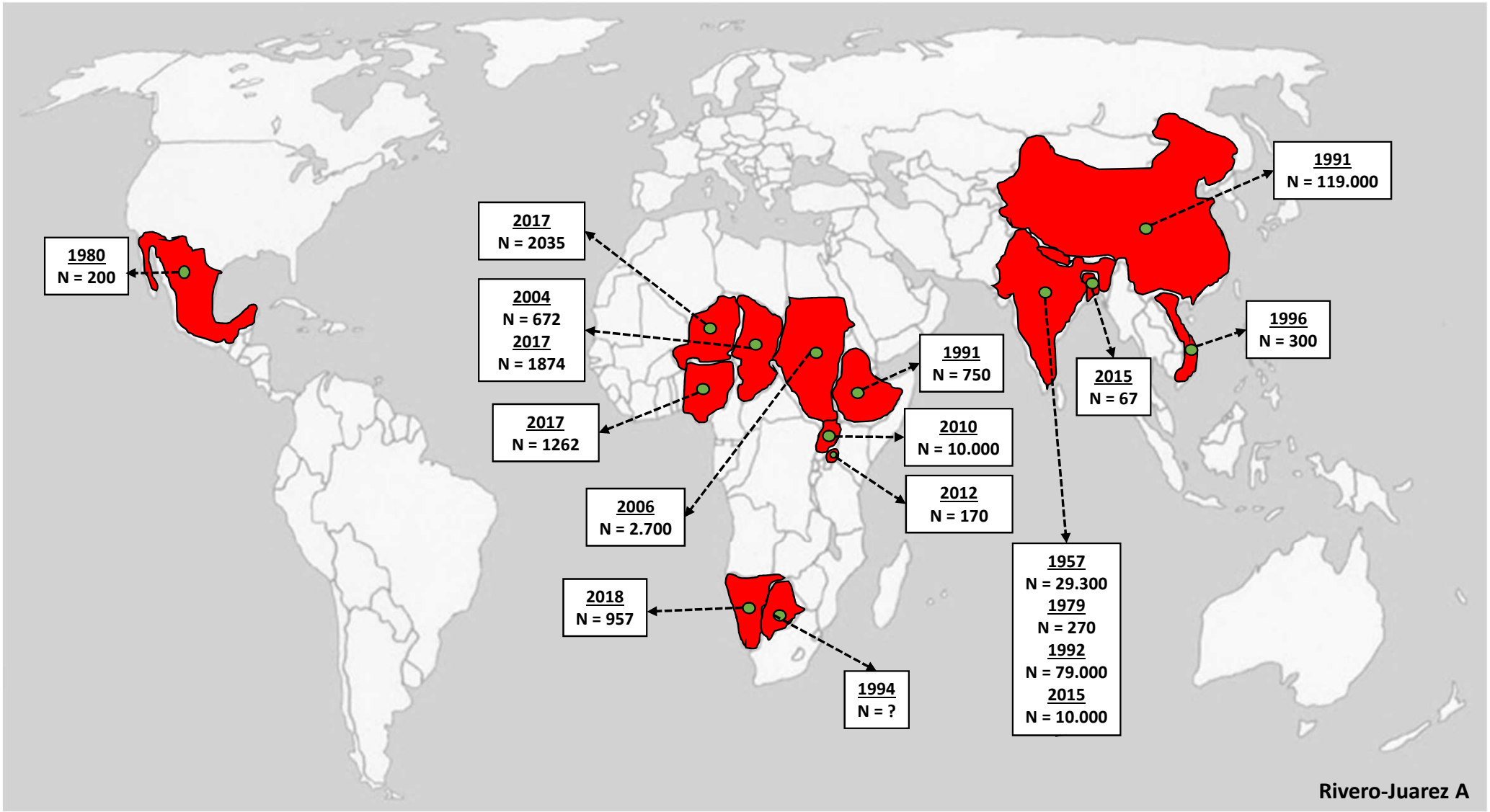
HEPATOLOGY AASLD

HEPATOLOGY, VOL. 00, NO. 00, 2016

Excretion of Infectious Hepatitis E Virus Into Milk in Cows Imposes High Risks of Zoonosis

Fen Huang,[1*] Yunlong Li,[1*] Wenhai Yu,[2*] Shenrong Jing,[1*] Jue Wang,[1] Feiyan Long,[1] Zhanlong He,[2] Chenchen Yang,[1] Yanhong Bi,[1] Wentao Cao,[1] Chengbo Liu,[1] Xuguo Hua,[3] and Qiuwei Pan[4]

Brotes epidémicos por el VHE



Brotes epidémicos en Cruceros

9news › health ›

HEALTH 3:53am February 23, 2017

Hepatitis E warning for passenger on two Melbourne cruises

By AAP

BBC Sign in News Sport Weather Capital TV Radio

NEWS LIVE BBC NEWS CHANNEL

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Page last updated at 13:00 GMT, Wednesday, 30 April 2008 14:00 UK

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Hepatitis E outbreak on P&O liner

Hundreds of holidaymakers are being tested for Hepatitis E after an outbreak onboard P&O liner Aurora.

The Aurora was at the centre of an outbreak of the Norovirus in 2003

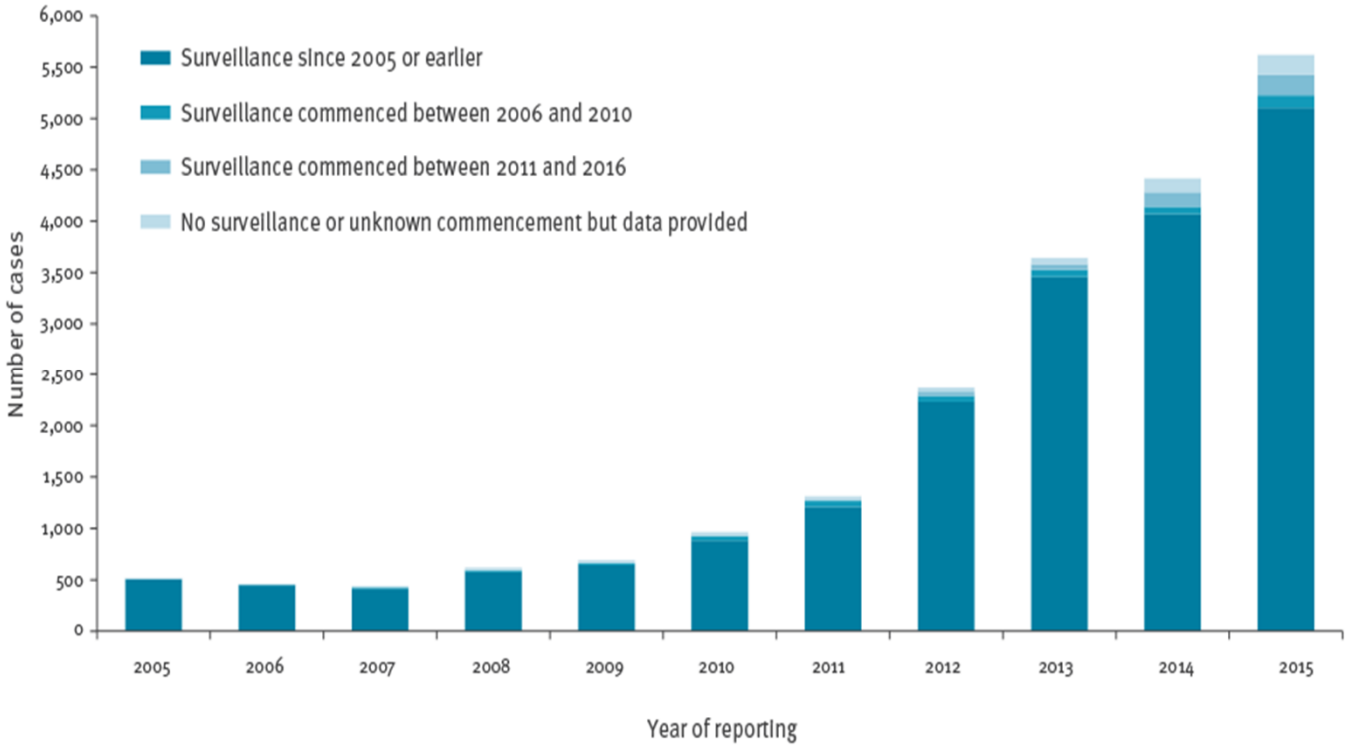
Seven passengers contracted the virus during an 11-week world cruise which ended in Southampton on 28 March.

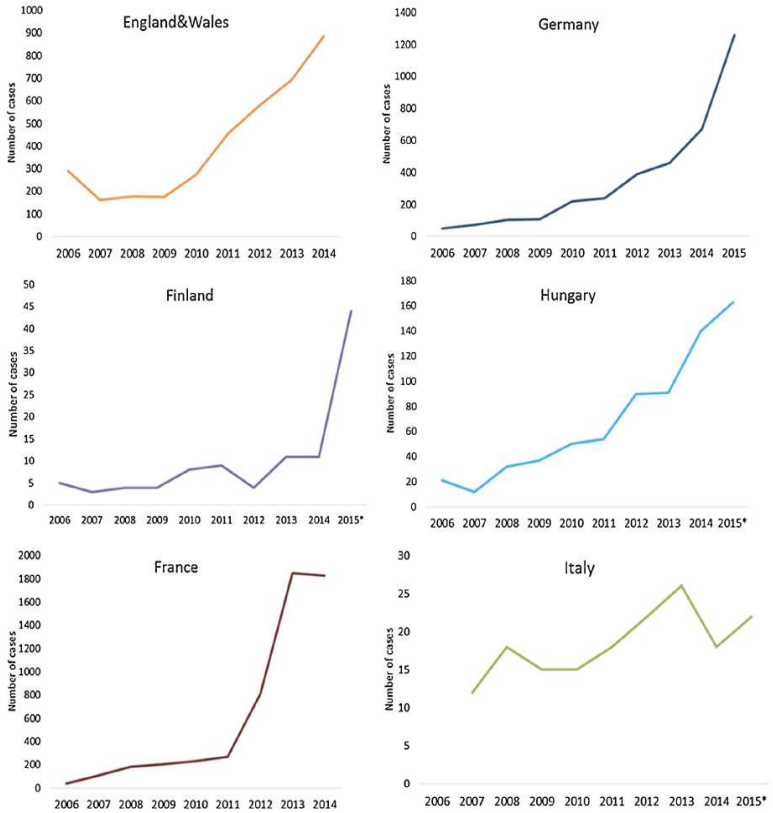
All the passengers onboard were sent a letter from the Health Protection Agency requesting a blood sample.

The HPA advises that the virus, which affects the liver, can be fatal but only in rare cases. P&O said it was cooperating fully with the inquiry.

It is thought the passengers caught the virus through eating or drinking contaminated food.

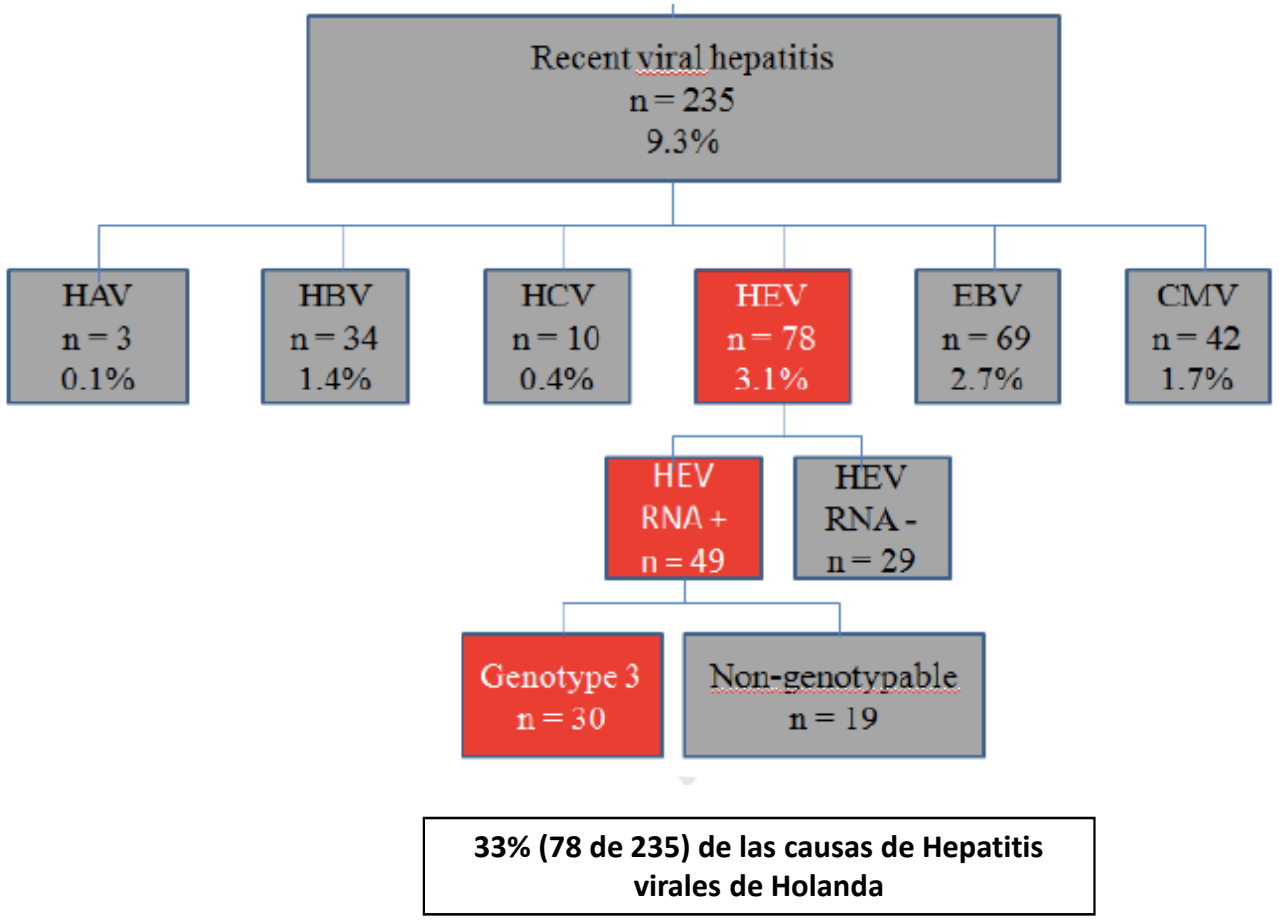
Aumento del número de casos en los últimos años





Aspinall et al Eurosurveillance 2017
Adlhoch et al J Virol 2016

Principal causa de hepatitis aguda viral en Holanda



33% (78 de 235) de las causas de Hepatitis virales de Holanda

Doting et Clin Microbiol Infect 2017

Clinical aspects: acute infection

- Acute HEV GT 3 infection is clinically silent in most patients
  - <5% may develop symptoms of acute hepatitis
    - Elevated liver enzymes, jaundice and non-specific symptoms*
- Immunocompetent patients clear the infection spontaneously
  - Progression to ALF is rare with HEV GT 3
  - ACLF occurs occasionally
- Non-sterilizing immunity develops after infection has cleared
  - Re-infection possible, but with lower risk of symptomatic hepatitis

Recommendations	Level of evidence	Grade of recommendation
Should test for HEV in: • All patients with symptoms consistent with acute hepatitis	A	1
Suggest testing for HEV in: • Patients with unexplained flares of chronic liver disease	C	2

*Fatigue, itching and nausea

EASL CPG HEV. J Hepatol 2018;doi: 10.1016/j.jhep.2018.03.005 [Epub ahead of print]

Clinical aspects: chronic infection

- Immunosuppressed patients can fail to clear HEV infection
  - Progression to chronic hepatitis*
- Immunosuppressed groups include:
  - Solid organ transplant recipients
    - ~50–66% of HEV-infected organ transplant recipients develop chronic hepatitis
  - Patients with haematological disorders
  - Individuals living with HIV
  - Patients with rheumatic disorders receiving heavy immunosuppression
- Most patients are asymptomatic and present with mild and persistent LFT abnormalities

Chronic HEV has mainly been described in the solid organ transplant setting

Recommendations	Grade of evidence	Grade of recommendation
Should test for HEV in: • All immunosuppressed patients with unexplained abnormal LFTs	A	1

*Persistence of HEV replication for 3 months. In rare cases, spontaneous clearance has been observed between 3 and 6 months

EASL CPG HEV. J Hepatol 2018;doi: 10.1016/j.jhep.2018.03.005 [Epub ahead of print]

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Extrahepatic manifestations

- Extrahepatic manifestations of HEV are increasingly recognized

Organ system	Clinical syndrome	Notes
Neurological	• Neuralgic amyotrophy* • Guillain–Barré syndrome* • Meningoencephalitis* • Mononeuritis multiplex • Myositis • Bell's palsy, vestibular neuritis and peripheral neuropathy	• ~150 cases of neurological injury (in HEV GT 3); mainly Europe • Most (>90%) cases in the immunocompetent **Most important**
Renal*	• Membranoproliferative and membranous glomerulonephritis • IgA nephropathy	• Mainly immunosuppressed GT 3-infected patients • Renal function improves and proteinuria levels decrease following HEV clearance
Haematological	• Thrombocytopenia • Monoclonal immunoglobulin • Cryoglobulinaemia • Aplastic anaemia† • Haemolytic anaemia†	• Mild thrombocytopenia is common; occasionally severe • Reported in 25% of cases of acute HEV in UK study • Occurs mainly in association with renal disease
Other	• Acute pancreatitis • Arthritis† • Myocarditis† • Autoimmune thyroiditis†	• 55 cases worldwide. HEV GT 1 only; usually mild

*There is good evidence to support a causal role for HEV and these associated conditions. For the other extrahepatic manifestations, causality remains to be established; †Case reports only

EASL CPG HEV. J Hepatol 2018;doi: 10.1016/j.jhep.2018.03.005 [Epub ahead of print]

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Laboratory diagnosis of HEV infection

- Acute HEV infection can be diagnosed by detection of anti-HEV antibodies
  - IgM, IgG or both by enzyme immunoassays in combination with HEV NAT
- Serological testing relies upon detection of anti-IgM and (rising) IgG

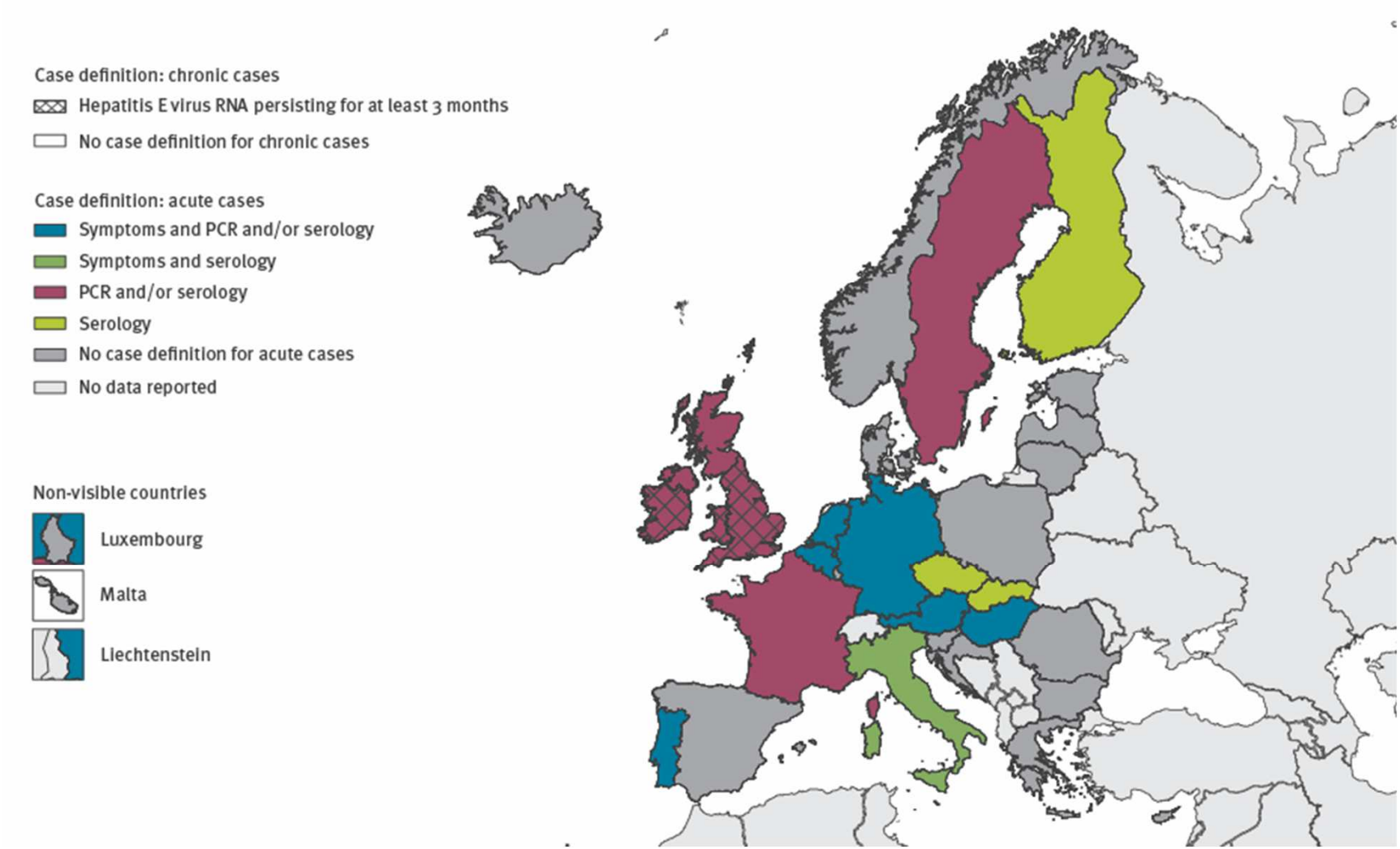
Infection status	Positive markers
Current infection – acute	• HEV RNA • HEV RNA + anti-HEV IgM • HEV RNA + anti-HEV IgG* • HEV RNA + anti-HEV IgM + anti-HEV IgG • Anti-HEV IgM + anti-HEV IgG (rising) • HEV antigen
Current infection – chronic	• HEV RNA (± anti-HEV) ≥3 months • HEV antigen
Past infection	• Anti-HEV IgG

*Patients with re-infection are typically anti-HEV IgM negative, but IgG and PCR positive

EASL CPG HEV. J Hepatol 2018;doi: 10.1016/j.jhep.2018.03.005 [Epub ahead of print]

EASL™ The Home of Hepatology

Sin Estrategia Nacional Diagnóstica



Aspinall et al Eurosurveillance 2017

Broadening testing for HEV

- Previously, only patients travelling to areas in Africa and Africa hyperendemic for HEV GT 1 or 2 were considered for testing
  - Now know that most HEV infection is locally acquired
- All patients presenting with hepatitis should be tested*
  - Irrespective of travel history

Immunological status	Patients who should be tested for HEV
Immunocompetent	• **Any patient with biochemical evidence of hepatitis*** • **Suspected drug-induced liver injury*** • Decompensated chronic liver disease† • Neuralgic amyotrophy† • Guillain–Barré syndrome† • Encephalitis† • Patients with unexplained acute neurology and raised ALT‡
Immunocompromised (developed countries)	• As above • Persistently abnormal ALT§

*Grade of evidence A, Grade of recommendation 1; †Testing should be done at disease onset, irrespective of ALT results; ‡Testing should be done at disease onset if ALT is abnormal; §If ALT is above the limit of normal on more than one occasion
EASL CPG HEV. J Hepatol 2018;doi: 10.1016/j.jhep.2018.03.005 [Epub ahead of print]

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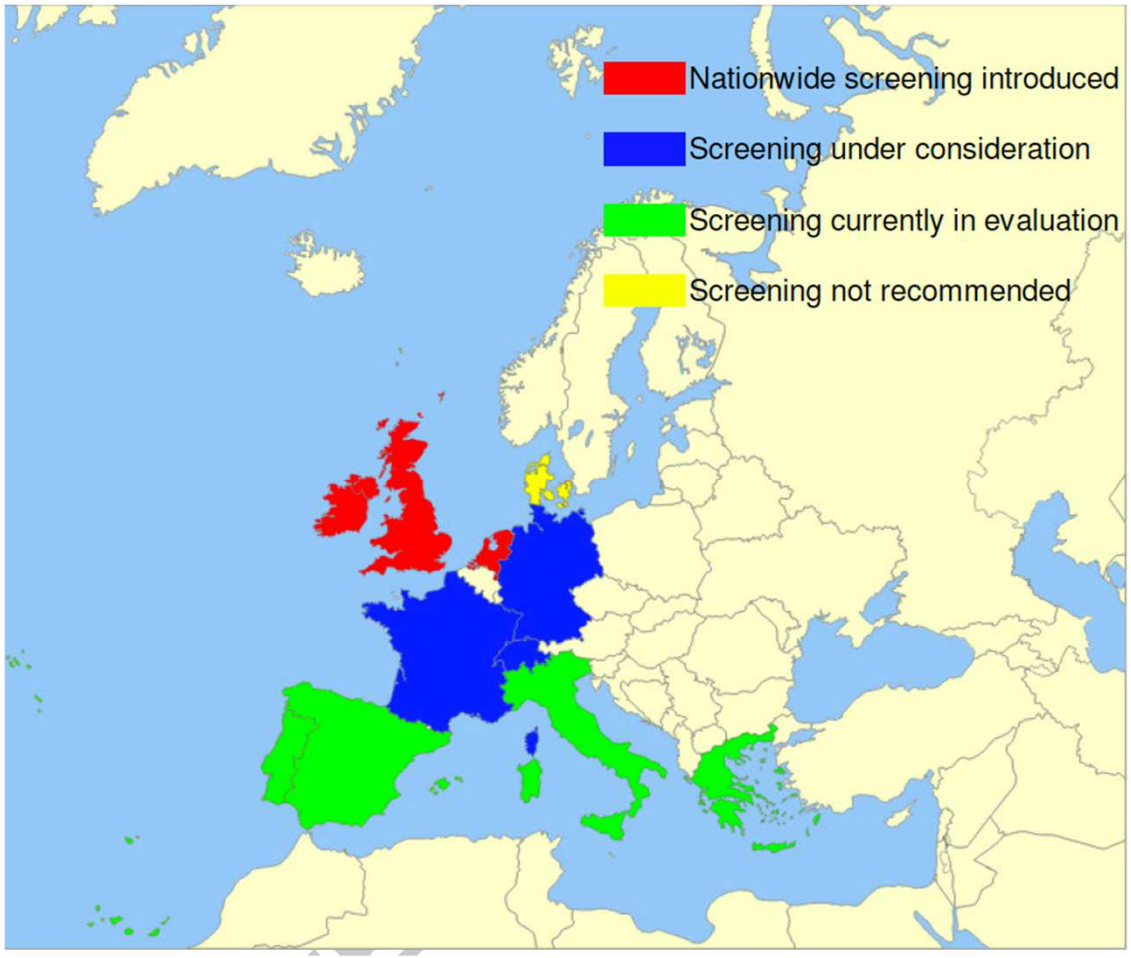
HEV: current situation regarding universal blood donor screening in different European countries



Mullhaupt B, et al. J Hepatol 2018 (In press)

Treatment of acute HEV infection

- Acute HEV infection does not usually require antiviral therapy*
- Most cases of HEV infection are spontaneously cleared
  - Some patients may progress to liver failure
  - Ribavirin
    - Early therapy of acute HEV may shorten course of disease and reduce overall morbidity

Recommendation	Grade of evidence	Grade of recommendation
• Ribavirin treatment may be considered in cases of severe acute hepatitis or acute-on-chronic liver failure	C	2

*Grade of evidence A

EASL CPG HEV. J Hepatol 2018;doi: 10.1016/j.jhep.2018.03.005 [Epub ahead of print]

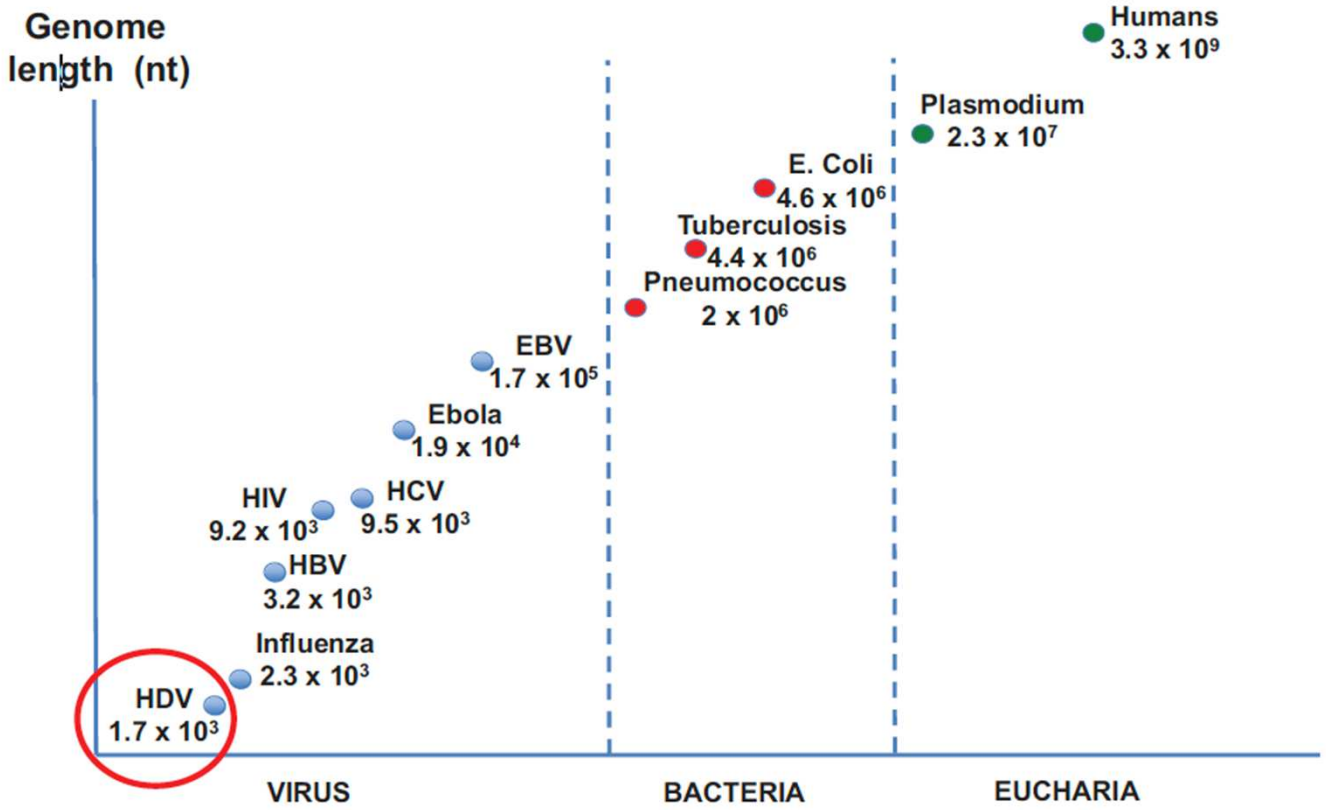
Caso

- Varón de 40 años, emigrante de origen turco
- Hepatitis B crónica diagnosticada en 2008.
- En tratamiento con lamivudina
- Remitido por ↑ significativo de ALT/AST y astenia.
- Bebedor de 60 gr. de alcohol al día.
- Relaciones sexuales de riesgo hace unos meses.
- No toma medicación potencialmente hepatotóxica
- Ecografía: Hígado nodular, de contorno irregular. Bazo 14 cms
- Fibroscan: 9,6 kPa
- Biopsia hepática: Cirrosis hepática
- Panendoscopia: Varices de pequeño tamaño sin riesgo de sangrado

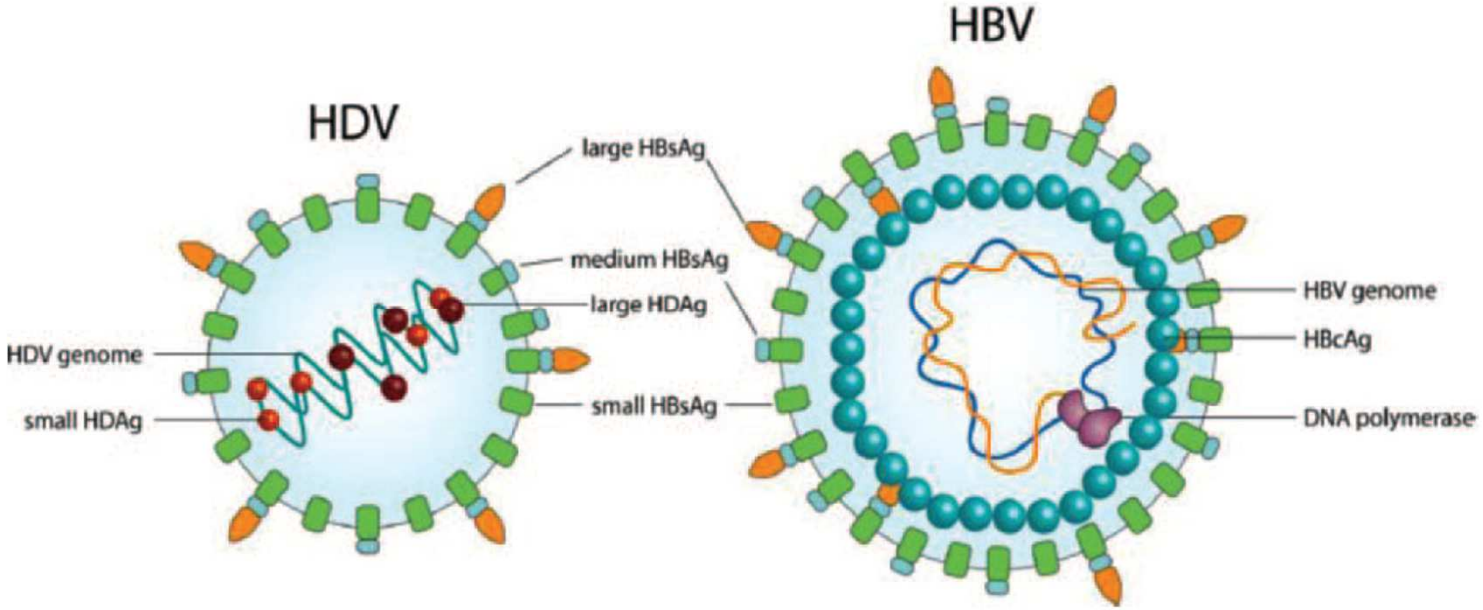
¿qué puede justificar la hipertransaminasemia y el deterioro hepático en este paciente?

1.- Reactivación del virus B
2.- Fármacos hepatotóxicos
3.- Ingesta continuada de alcohol
4.- Hepatitis autoinmune
5.- Infección por virus delta

Genome size of living organisms



Virion structure for hepatitis B and D viruses



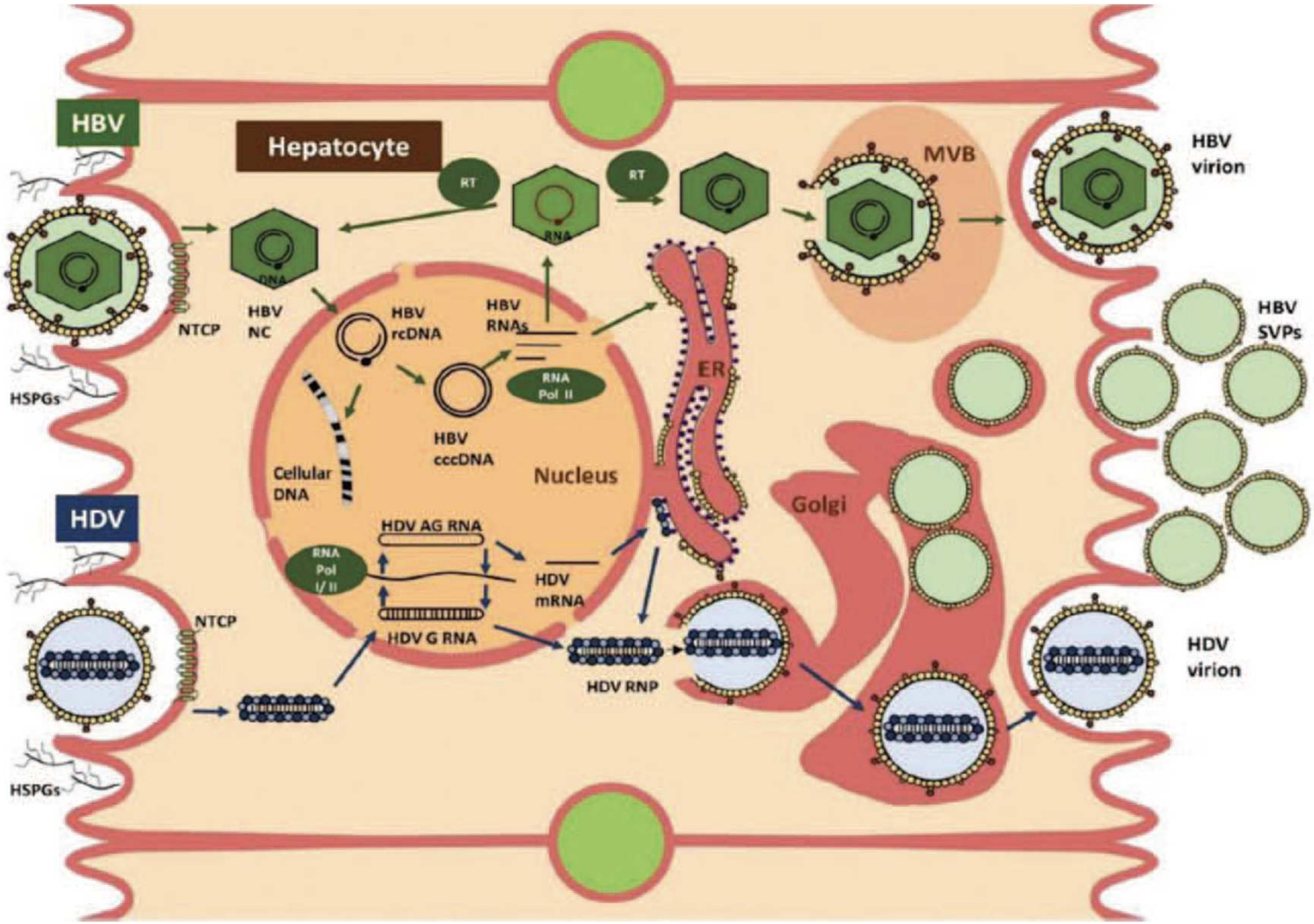
- Defective virus - presence of HBV is required for virion assembly and secretion
- Individuals with HDV are always dually infected with HDV and HBV
- HBV replication is suppressed in most HDV-infected individuals
- The only antigen associated with HDV is the HDAg (two forms)
- The lipoprotein envelope of HDV is provided by the HBV

Alfaiate D, et al. Antivir Res 2015; 122:112–129.

HDV life cycle

NTCP*
Receptor for both HDV and HBV

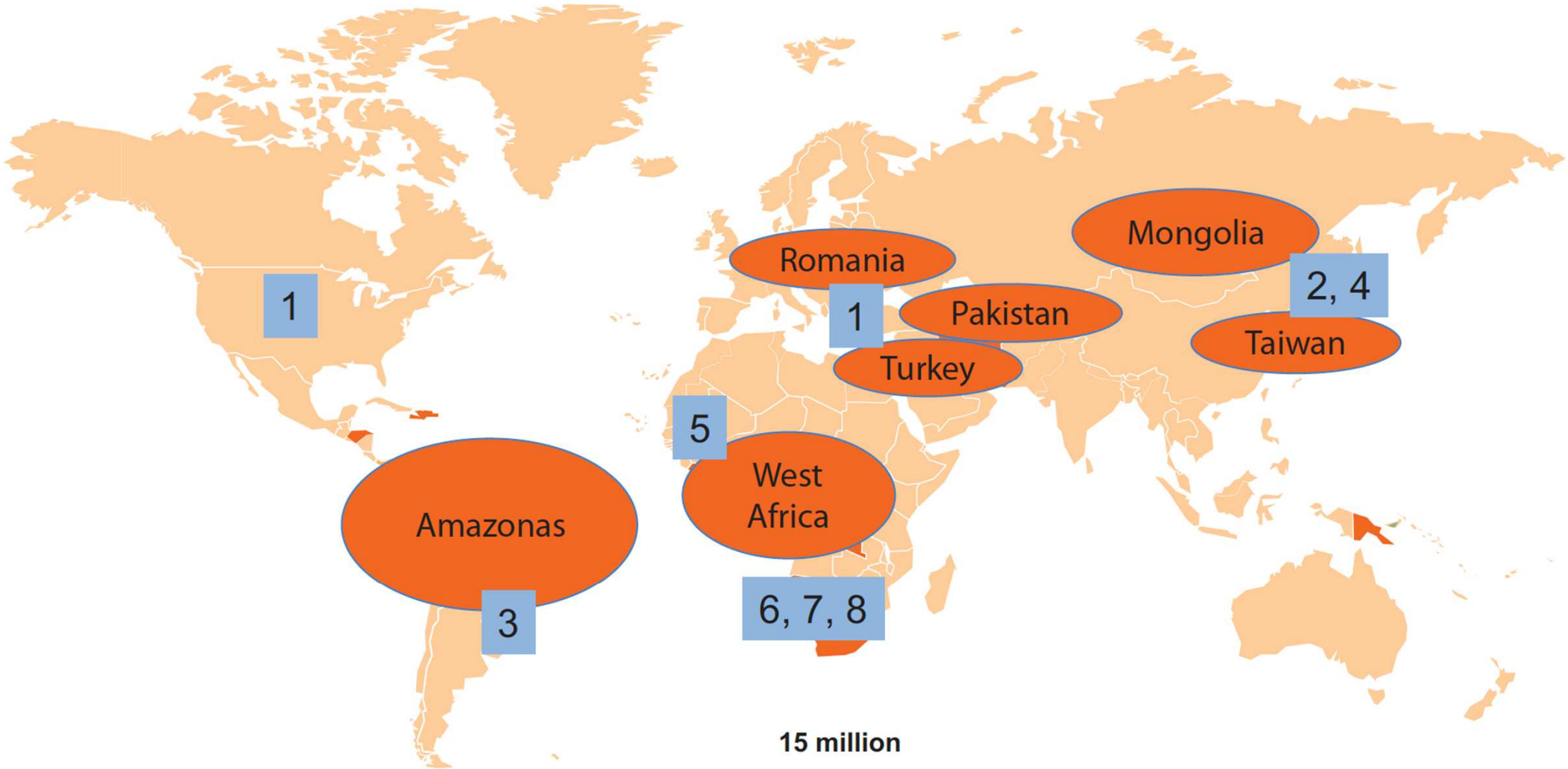
*Sodium Taurocolate Cotransporting Polypetide



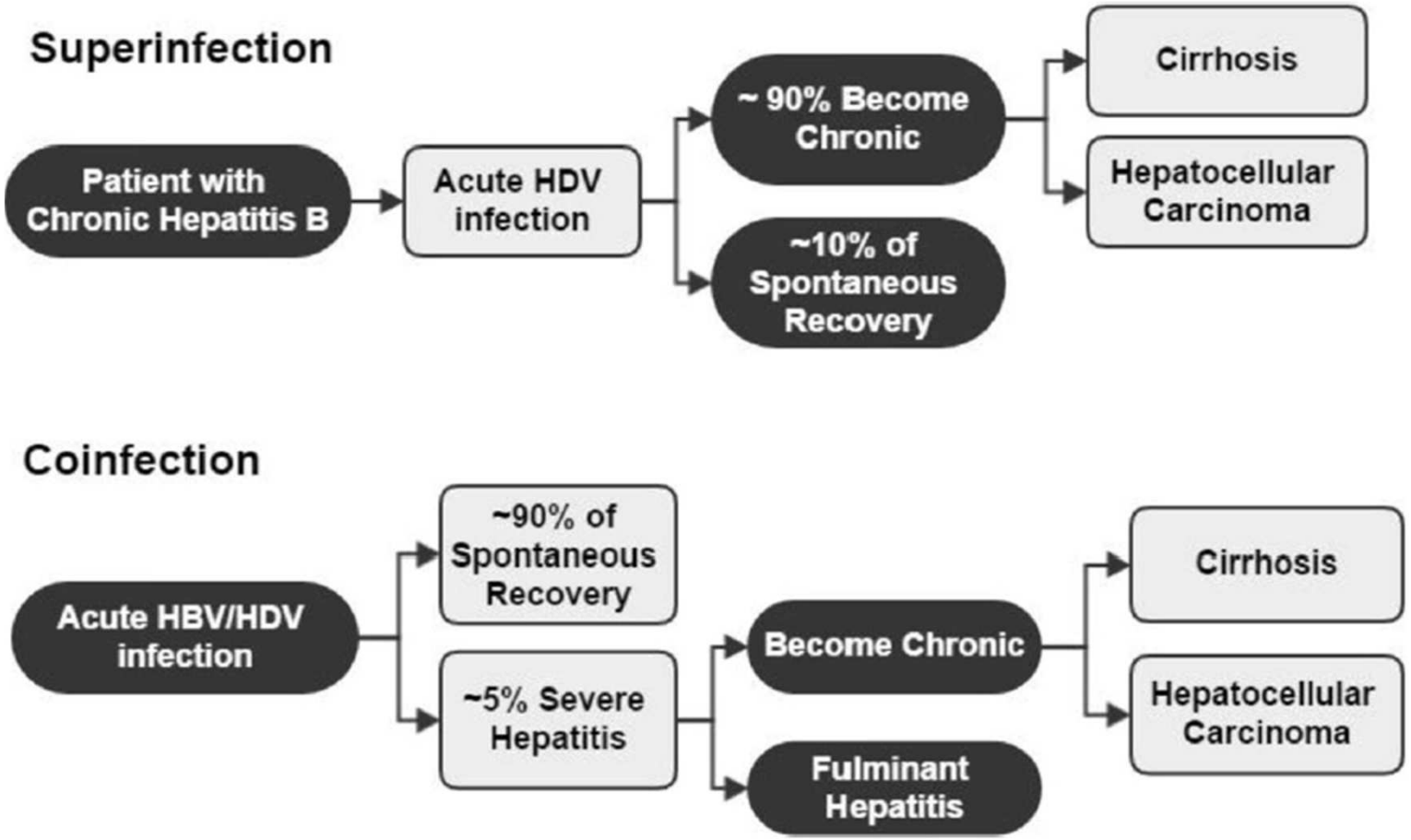
Alfaiate D, et al. Antivir Res 2015; 122:112–129.

HDV epidemiology

- **G1:** predominant in the western world
- **G2:** predominant in the Far East
- **G3:** outbreaks with high incidence of liver failure in South America
- Endemic in the Mediterranean basin



Clinical course of hepatitis Delta



Botelho-Souza et al. Virology Journal (2017) 14:177

Diagnosis of HDV infection

Diagnostic markers	Acute HBV/HDV coinfection	Acute HDV superinfection	Chronic HDV infection
HBsAg	Positive	Positive	Positive
Anti-HBc, IgM	Positive	Negative	Negative
Serum HDAg (by EIA/RIA)	Early and short-lived, frequently missed	Early and transient, and frequently missed	Not detectable
Serum HDV RNA (by hybridization)	Early, transient but last longer than HDAg	Early and persistent	Usually positive
Anti-HDV, total	Late, low titer	Rapidly increasing titers	High titers
Anti-HDV, IgM	Transient, may be the only marker	Rapidly increasing and persistent titers	Variable titers, usually high
Liver HDAg	Not indicated	Positive	Usually positive, may be negative in late stages

No FDA or EMA-licensed viral load test
Diagnosis (HDV-Ab) often missed in HBsAg-positive patients

HBsAg-Positive Persons at High Risk of HDV Infection Who Should Be Screened

- Persons born in regions with reported high HDV endemicity*
- Persons who have ever injected drugs
- Men who have sex with men
- Individuals infected with HCV or HIV
- Persons with multiple sexual partners or any history of sexually transmitted disease
- Individuals with elevated ALT or AST with low or undetectable HBV DNA

*Africa (West Africa, horn of Africa), Asia (Central and Northern Asia, Vietnam, Mongolia, Pakistan, Japan, Taiwan), Pacific Islands (Kiribati, Nauru), Middle East (all countries), Eastern Europe (Eastern Mediterranean regions, Turkey), South America (Amazonian basin), Other (Greenland)

AASLD 2018 Hepatitis B Guidance. Hepatology 2018; 67: 1560-1599

Treatment of HDV

- Peg-IFNα is the drug of choice
  - Without clear differences in efficacy between peg-IFNα 2a or α2b
- Undetectable HDV RNA 24 wks after completing treatment, ranges from 23% to 57%.
- ALT normalization typically parallels the virological responses.
- The combination of nucleosid(t)e analogues (NA) with Peg-IFNα does not increase the likelihood of an off treatment virological response.
- Late relapses can occur with longer follow-up
  - Very low rates of sustained HDV-RNA undetectability.

AASLD 2018 Hepatitis B Guidance. Hepatology 2018; 67: 1560-1599

Antiviral Treatment and Liver-Related Complications in Hepatitis Delta

Retrospective single-center cohort

136 anti-HDV+ patients (45% cirrhosis)

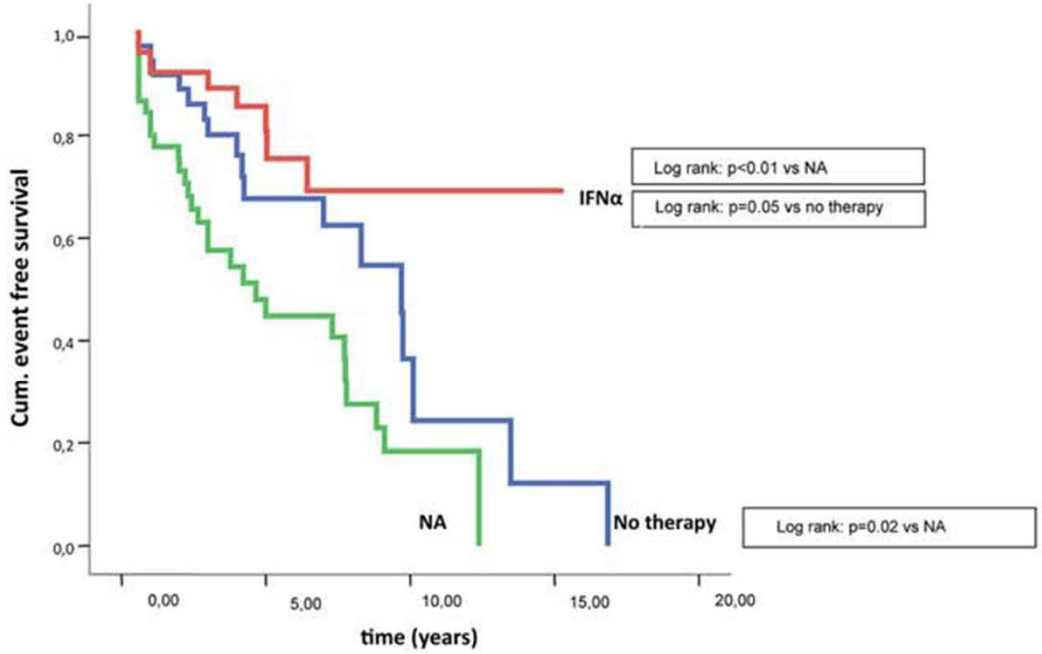
Treatment

- 29% none
- 38% IFNa-based therapies,
- 33% nucleos(t)ide analogues (NAs)

Mean FU, 5.2 years

Clinical endpoints

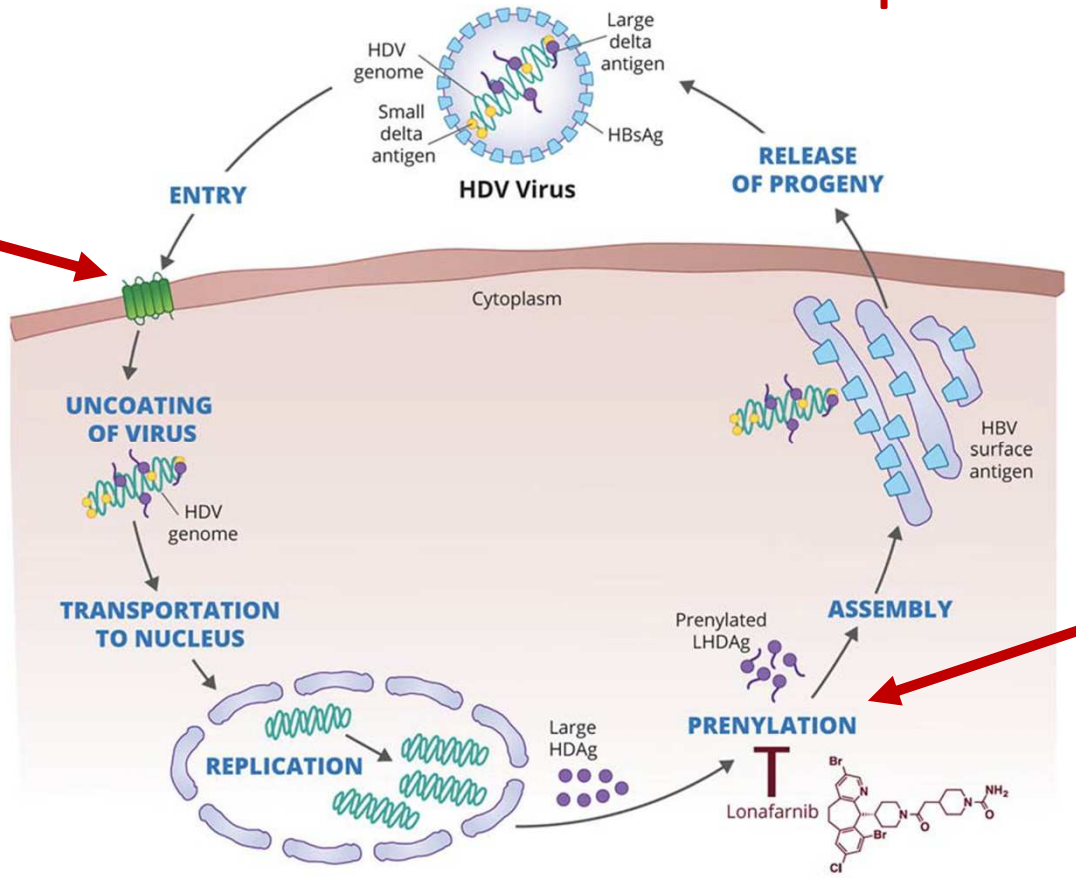
- Decompensation
- Hepatocellular carcinoma
- Transplantation
- Liver-related death.



Wranke A, et al. Hepatology 2017; 65: 414-425

Experimental treatments for hepatitis delta

HDV entry inhibitors
- Myrcludex B
- Vanitaracin A



Prenylation inhibitors
- Lonafarnib
- FTI-277
- FTI-2153

Etzion O. Hepatology 2018; 67: 1198

Prevention

The best strategy to prevent hepatitis D is HBV vaccination