

O vírus da hepatite E causa doença crônica Novidades do EASL 2012

***VI Workshop Internacional de
Atualização em Hepatologia
Curitiba – agosto 2012***

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EASL | THE INTERNATIONAL
LIVER CONGRESS™ 2012

57th ANNUAL MEETING OF THE EUROPEAN ASSOCIATION FOR THE STUDY OF THE LIVER



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C

Cornwall

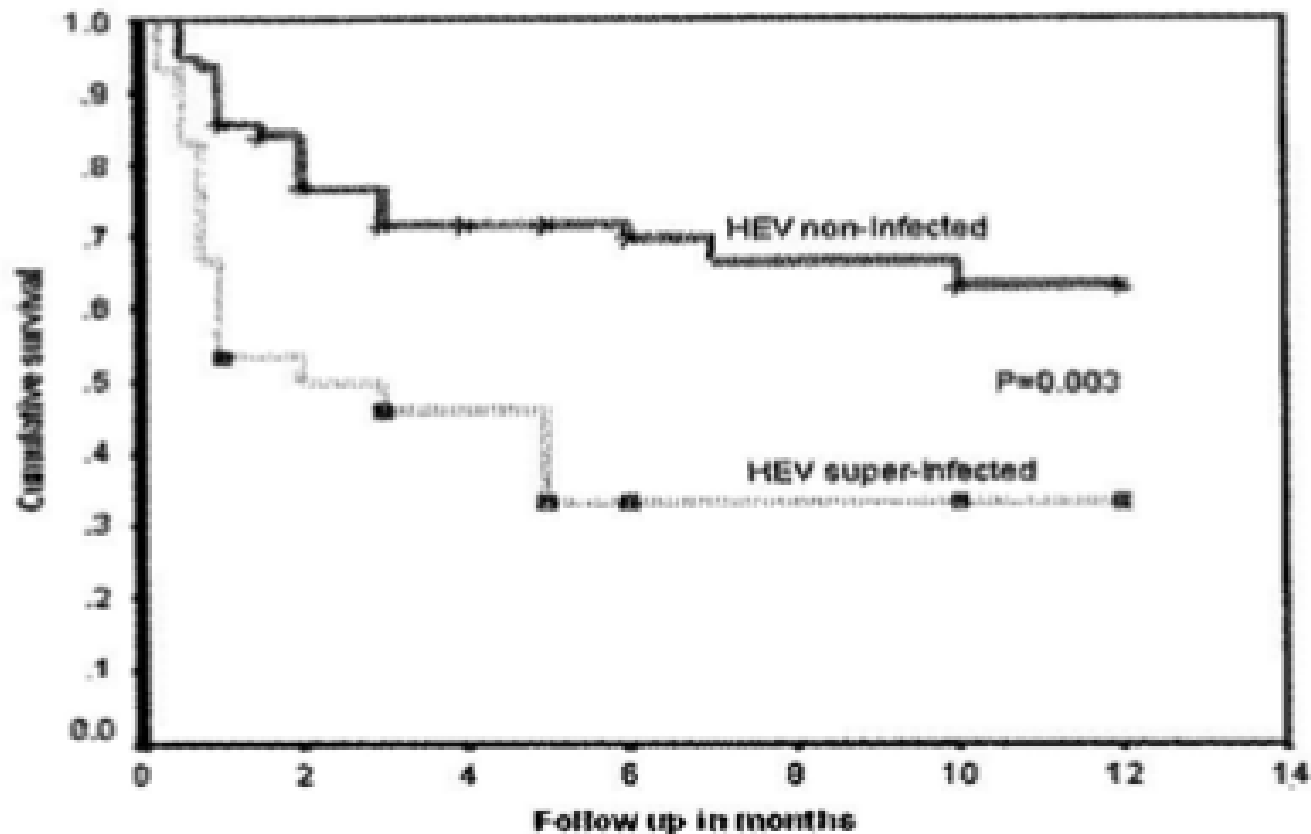




**Mortalidade de 25% em
mulheres grávidas**

70% mortalidade em hepatopata crônico

HEV: in chronic liver disease



Vírus da Hepatite E

1983 Primeira observação do vírus

Balayan MS. Intervirology

1990 Clonagem e sequenciamento

Reyes RG. Science

1991 Primeiro teste sorológico

Yarbough PO. J Virology

1994 Zoonose

Meng XJ. Proc Natl Acad Sci USA

Vírus da Hepatite E

2008 Hepatite E crônica

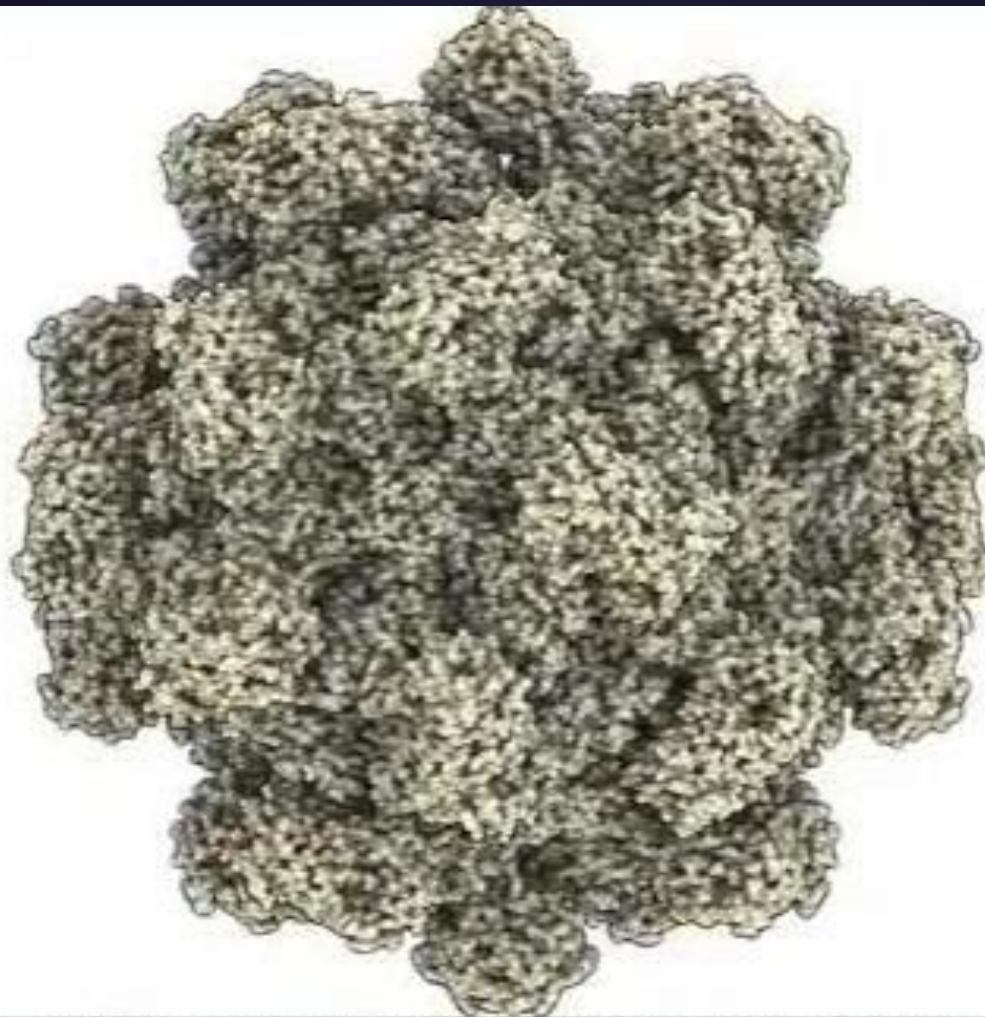
Kamar N. NEJM

2010 Ribavirina para Hepatite E

Reyes RG. Science

2010 Fase 3 vacina recombinante

Zhu FC. Lancet



Hepatitis E virus ORF2 (Genotype 3) - PDB 2ZTN - Quttemol image © 2010 JYS

Yamashita, T. et al. Proc.Natl.Acad.Sci.USA 106: 12986 - 12991

Epidemiologia

Problema grave em países em desenvolvimento

Transmissão fecal oral

Afeta adultos jovens

Mortalidade de 25% em mulheres grávidas

Epidemiologia

Semelhante a hepatite A

Frequente em viajantes

Raramente em não-viajantes

Pouca relevância em países desenvolvidos

Epidemiologia

~~Semelhante a hepatite A~~

~~Frequente em viajantes~~

~~Raramente em não-viajantes~~

~~Pouca relevância em países desenvolvidos~~

Conceitos atuais

68 casos HEV não viajantes, **genótipo 3**

H:M = 3:1

Caucasianos

Idade 63.5 (35 -92 a)

2007

Dalton et al. J Viral Hepatitis

Dalton et al. European J Gastro 2008

Demografia

HEV

demographics and outcome

	UK <i>Dalton et al 2008</i>	France <i>Peron et al 2006</i>	Japan <i>Okamoto et al 2003</i>
Cases	40	23	46
Mean age	65 yrs	54.4 yrs	59.6 yrs
% males	77.5%	73.9%	87%
Deaths	7.5%	8.7%	10.8%
Liver deaths	5%	8.7%	10.8%



HEV in animals

- Genotype 3 (& 4):
 - Human disease
 - Found in animals (asymptomatic)
 - Pigs
 - Worldwide
 - 85% UK pigs affected
 - 20% of pig herd excrete HEV in faeces
 - Boar, deer, rats, rabbits, cut-throat trout





HEV 3: Asymptomatic infection

- Asymptomatic infection probably very common
- Aurora outbreak 2008
 - 33 cases hepatitis E
 - HEV 3: identical on sequencing
 - Foodborne outbreak
 - Source uncertain
 - ?shellfish
 - **>50% asymptomatic**

Said et al EmlnfDis 2009



Hepatite Aguda Gen3

Assintomática - doença leve – lesão fulminante

**Maioria recupera em 4 a 6 semanas
Idade 63.5 (35 -92 a)**

Dalton et al. Lancet 2007

Peron et al. J. Viral Hepatology 2007

Países Desenvovidos

- **USA** Halbur *JClinMicro* 2001
- Japan Miuzo *ClinMicro* 2002
- **France** Mansuy *JMedViro* 2004
- Netherlands Widdowson *JMedViro* 2004
- Spain Buti *JViroMethods* 1995
- Italy Romano *J Hepatol* 2010
- New Zealand Dalton *JGastHepatol* 2007
- Denmark, Germany, Hungary, Sweden 2009-10

Zoonose

HEV: a zoonosis

- Close sequence homology of HEV in pigs and humans

Menget al ProcNatAcadSci 1997

- High seroprevalence in swine handlers

Meng et al JClinMicro 2002

- Cases caused by eating HEV infected meat

Teiet al Lancet 2003



Places HEV hides (1): Drug-induced liver injury (DILI)

- 13% of patients with DILI have HEV3
Dalton et al APTherap 2007
- USA: 3% of DILI is HEV3 infection
Davern et al Gastroenterol 2011
- Diagnosis of DILI not secure without testing for HEV



Places HEV hides (2): with the Neurologist

- HEV is neuropathogenic:
 - inflammatory polyradiculopathy
 - Guillain-Barré syndrome
 - bilateral brachial neuritis
 - ataxia/proximal myopathy
- **LFTs only mildly abnormal and most cases anicteric**
- Occurs in: acute and chronic HEV
- Outcome: most recover, some do not

Kamar et al Emerg Inf Dis 2011

Places HEV hides (3): immunosuppressed patients

- Chronic HEV in immunosuppressed:
 - Transplant patients
 - HIV
- **Asymptomatic**
- **ALT 100 -300**

Kamar et al NEJM 2008

Gerolami et al NEJM 2008

Haagsma et al LivTrans 2008

Dalton et al NewEngJMed 2009

Places HEV hides (4): blood supply

- Post transfusion hepatitis E reported in several countries

Boxall et al Transfusion Med 2006

Colson et al EmergInfDis 2007

Matsubayashi et al Transfusion 2004

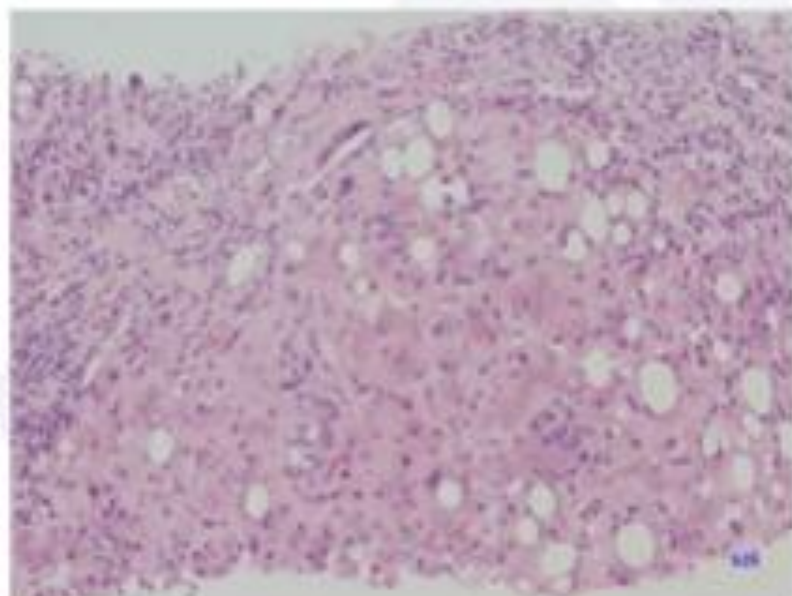
- 0.7% mini-pools in UK donors are HEV PCR +ve

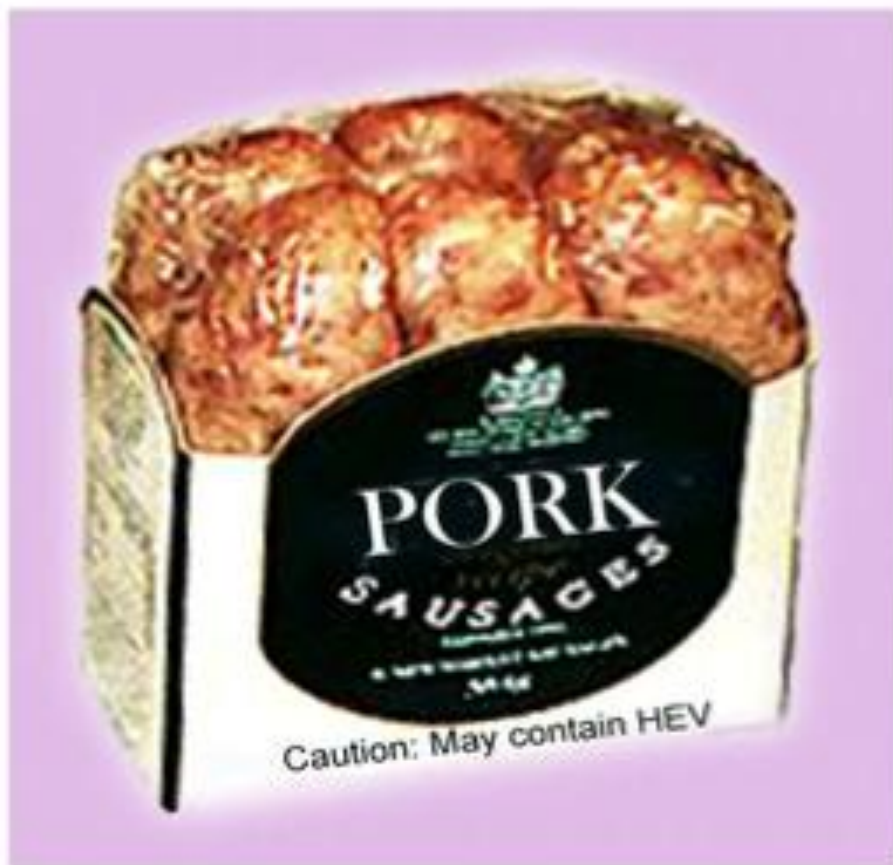
Ijaz et al VoxSang 2011

- Unrecognised infection is occurring:
 - HEV not tested in donors

Places HEV hides (5): patients with decompensated chronic liver disease

- 76 yr old male
- Alcohol 35U/week
- Decompensated +++
 - Bilirubin 86
 - ALT 2286
- Transferred to another hospital
- Died at 4 months of
'decompensated alcoholic liver
disease due to alcoholic hepatitis'







HEV — Immunocompromised patients

Jean-Marie Peron, MD, PhD (France)

Hepatitis E virus in the immunocompromised patient

- Patients receiving chemotherapy for malignant disease
- Solid organ transplant recipients
- Patients infected with HIV
- Treatment of chronic hepatitis E

Conclusion

1. HEV infection markers should be included in the diagnostic workup of elevated transaminases in immunocompromised patients
2. PCR based detection of hepatitis E viral RNA is essential to make the diagnosis
3. There is a risk of patient to patient transmission of HEV
4. Chronic HEV infection is possible, including evolution towards cirrhosis, especially in solid organ graft recipients
5. First line therapeutic approach : reduce doses of immunosuppressive drugs such as tacrolimus
6. Second line therapeutic approach should probably be ribavirin



HEV — Vaccine

Rakesh Aggarwal, MD (India)

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