

hepatitis E bij de immuungecompromitteerde patiënt

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Disclosure of interests of Hans Zaaijer

No conflicts of interests:

Hans Zaaijer is or was paid for
unrestricted lectures and teaching by:
ACTA, Abbott, Gilead, Griffols, ISBT,
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No consultancy, no advisory boards, no shares,
or other interests in companies.



'hepatitis E' bestaat niet

"hepatitis E" = 2 ziekte entiteiten

1) a tropical disease

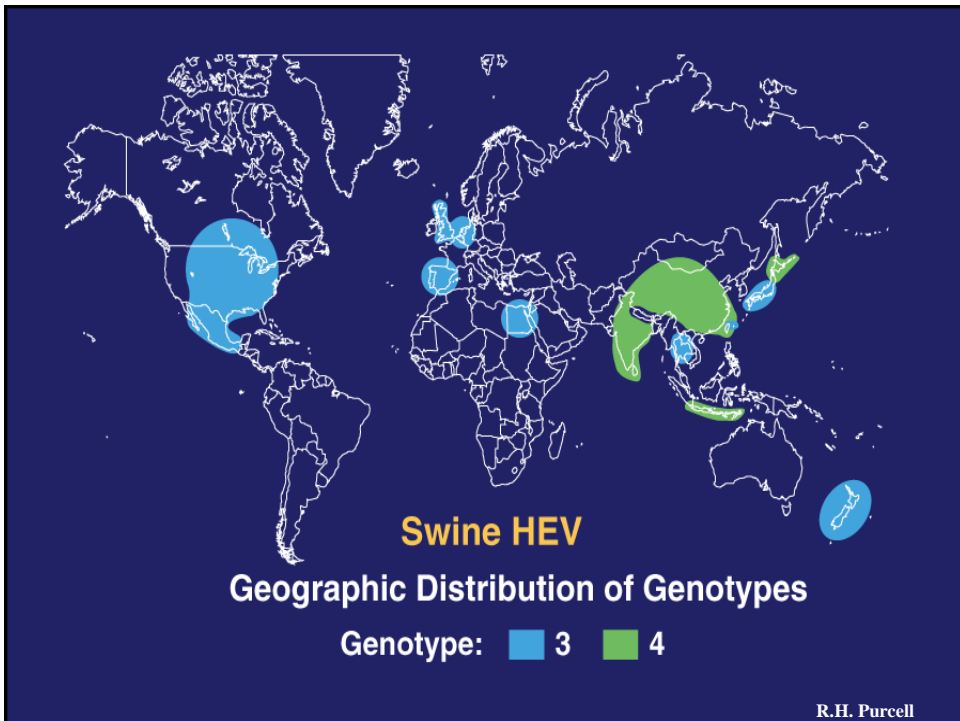
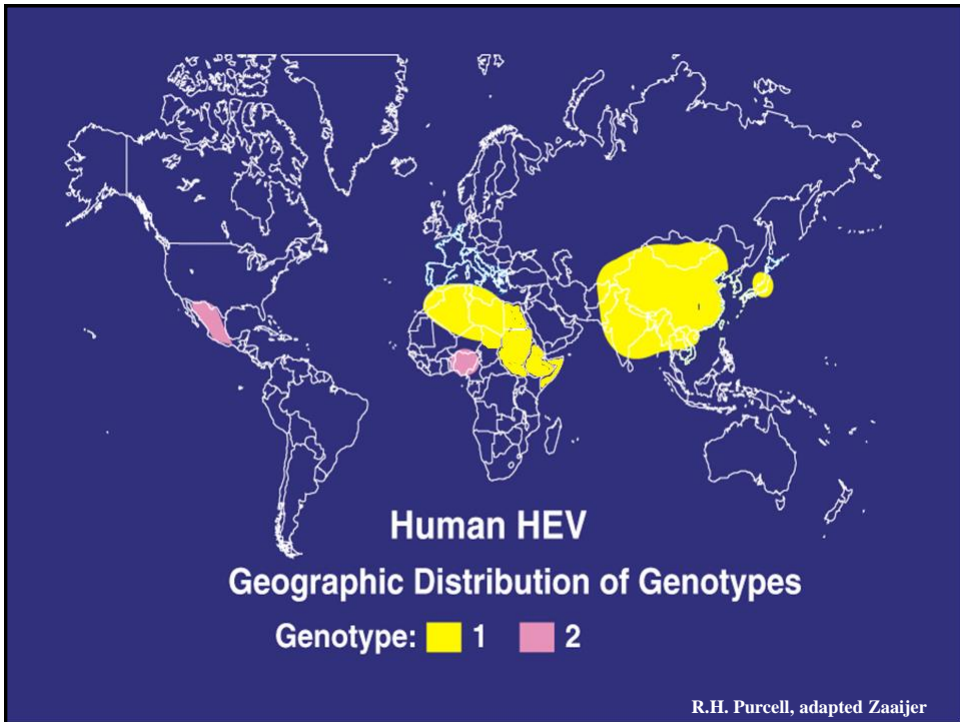
- acute (often severe) hepatitis.
- caused by the human viruses HEV genotype 1 and 2.
- feco-oral transmission, water-borne outbreaks.
- high mortality among pregnant women.
- your previously healthy back-packer, returning from India with fulminant hep E, may need liver transplantation.

2) a silent outbreak in temperate regions

- zoonotic infection by the animal viruses HEV genotype 3 and 4.
- in most cases asymptomatic.
- sometimes mild hepatitis in elderly (men).
- chronic hepatitis in SOT and SCT patients, cause cirrhosis.
- food-borne transmission (undercooked pork and deer).
- no mortality among pregnant women.
- in NL majority of pigs acquire infection, at slaughter 10% of pig livers is HEV+

"hepatitis E" = 2 ziektes

	tropical & travellers hep E HEV genotypes 1,2	zoonotic (pigs) hep E HEV genotype 3
pregnant women	20% fatality	no disease
children	acute hepatitis	no disease
adults	acute hepatitis	'no disease'
middle aged, elderly	acute hepatitis	acute hepatitis (mild)
extra hepatic:	?	- sporadic: neuralgic amyotrophy - GBS ?
organ/SC Tx patients	?	chronic hepatitis, cirrhosis



Belangrijk

Laboratorium diagnostiek van hepatitis E

- 1) acute hepatitis E *zonder* onderliggend lijden, onafhankelijk van tropisch/import of inheems/zoonotisch: vertrouw op (moderne) serologie: HEV IgG en IgM.
- 2) acute of chronische hepatitis E,
bij immuunsuppressie, -modulatie, -deficiëntie:
direct HEV RNA PCR.
HEV antistoffen blijven regelmatig jarenlang diep negatief.

een stokpaard van Zaaijer:

serologie op CMV, HEV ed. na SOT/SCT: kunstfout & ongelukken; direct PCRs doen.

hepatitis E bij de immuungecompromitteerde patiënt

dit betreft HEV genotype 3,
geen ervaring met HEV genotypes 1,2,4

Therapeutische opties chron. hep E (gt3):

- stapsgewijs verminderen immunosuppressie
- ribavirine
- interferon (niet na orgaan Tx)
- sofosbuvir? (dosis? hoelang?)

Therapeutische opties acute hep E (gt3):

- ribavirine¹

1 Peron ea., Liver Int 2016; 36: 328-333:

...conclude that treatment of acute HEV infection using ribavirin is safe and that short-term treatment tailored to viraemia is best regimen for this indication. Ribavirin could be an effective therapeutic option for patients with acute HEV infection in specific situations: (1) older patients, (2) underlying liver disease, (3) undergoing chemotherapy, (4) those receiving immunosuppressive treatments for autoimmune disease.

Dosering ribavirine bij chron. hep E:

? zomogelijk 12mg/kg/dag, in 2 doses ?

1 Kamar N, ea. Ribavirin for chronic hepatitis E virus infection in transplant recipients. NEJM 2014;370:1111-20:

... We examined records of 59 patients who had received a solid-organ transplant. Ribavirin therapy was initiated a median of 9 months (range 1-82) after the diagnosis of HEV infection at a median dose of 600 mg per day (range, 29 to 1200) ...

2 Dalton & Kamar. Treatment of hepatitis E virus. Curr Opin Infect Dis 2016; 29(6): 639-644.

geen uitsluitel over dosering ribavirine

Behandeling van hepatitis E (gt3)

	hematology, rheumatology patients	solid organ transplant patients
acute hep E	wait for 3 months; or immediate ribavirin ¹	wait for 3 months; or immediate ribavirin ¹
chronic hep E	if possible: reduce imm.sup.	if possible: reduce imm.sup.
(ribavirin: 12 mg/kg/day, in 2 doses)	ribavirin	ribavirin
	interferon	
	(sofosbuvir?)	(sofosbuvir?)

¹ Peron ea., *Liver Int* 2016; 36: 328-333:

We conclude that the treatment of acute HEV infection using ribavirin is safe and that short-term treatment tailored to viraemia is the best regimen for this indication. Ribavirin could be an effective therapeutic option for patients with acute HEV infection in specific situations:

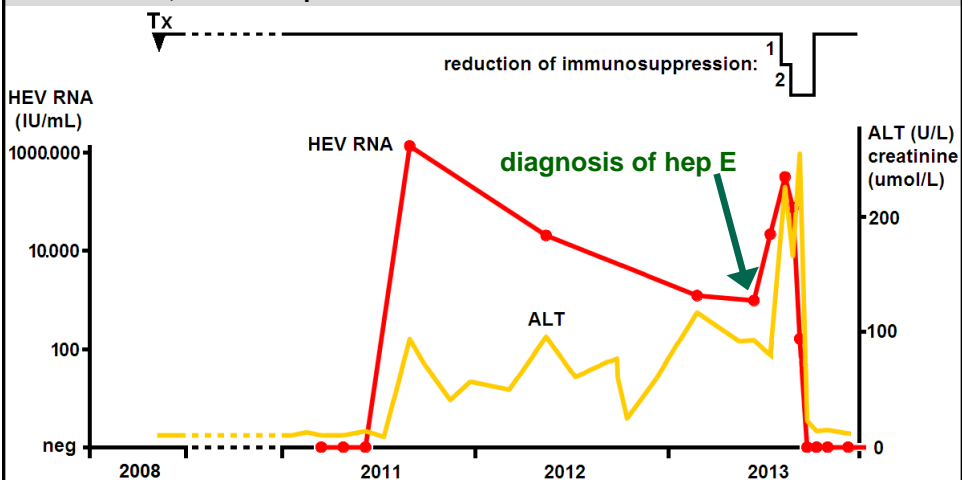
(1) older patients, (2) patients with underlying liver disease, (3) patients undergoing chemotherapy or (4) those receiving immunosuppressive treatments for an autoimmune disease.

Boy A, 8 yrs.

2006: pneumococcal infection → HUS → kidney Tx

2011: chronic hepatitis : 'drug induced liver injury' (dili)

2013: no dili, chronic hepatitis E !



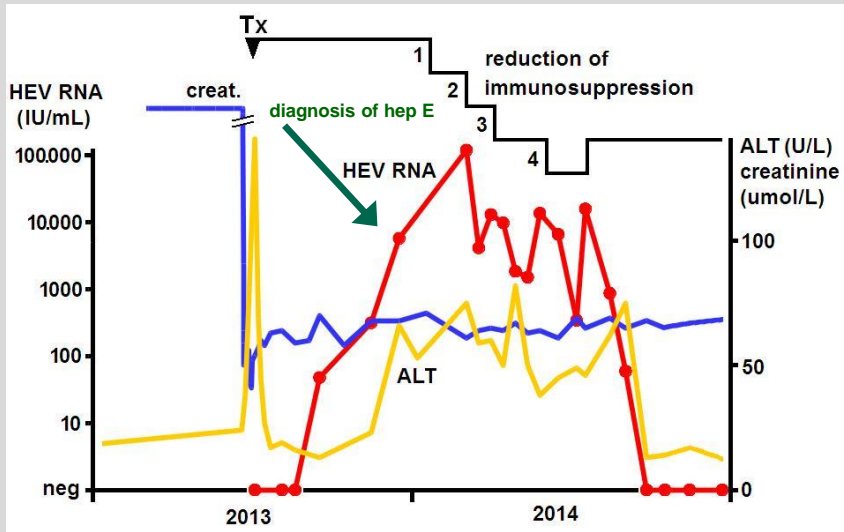
step 1 = mycophenolate mofetil: 800 to 600 mg/m²/day

step 2 = tacrolimus: 0.1 to 0.05 mg/kg/day

prednisolone remained unchanged at 2 mg/m²/day

Bouts ea. *Pediatrics* 2015, vol 135, nr 4

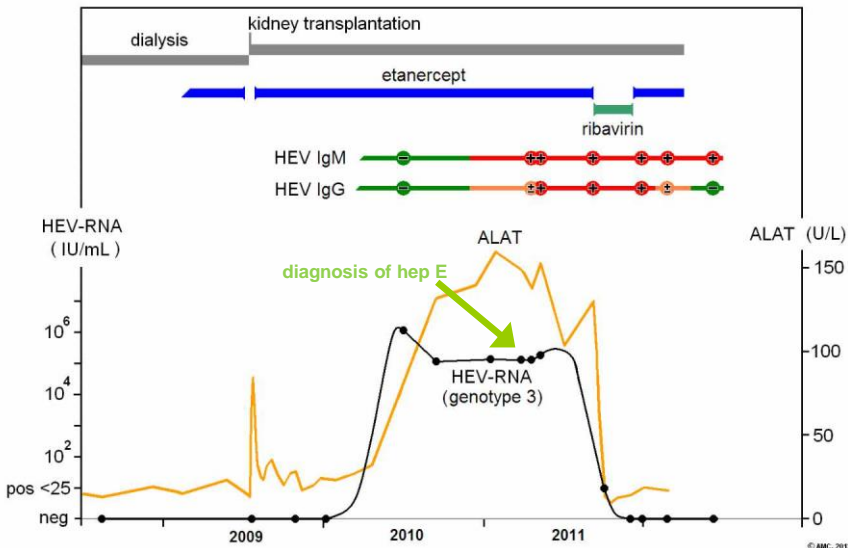
girl B, 11 yrs kidney failure e.c.i.



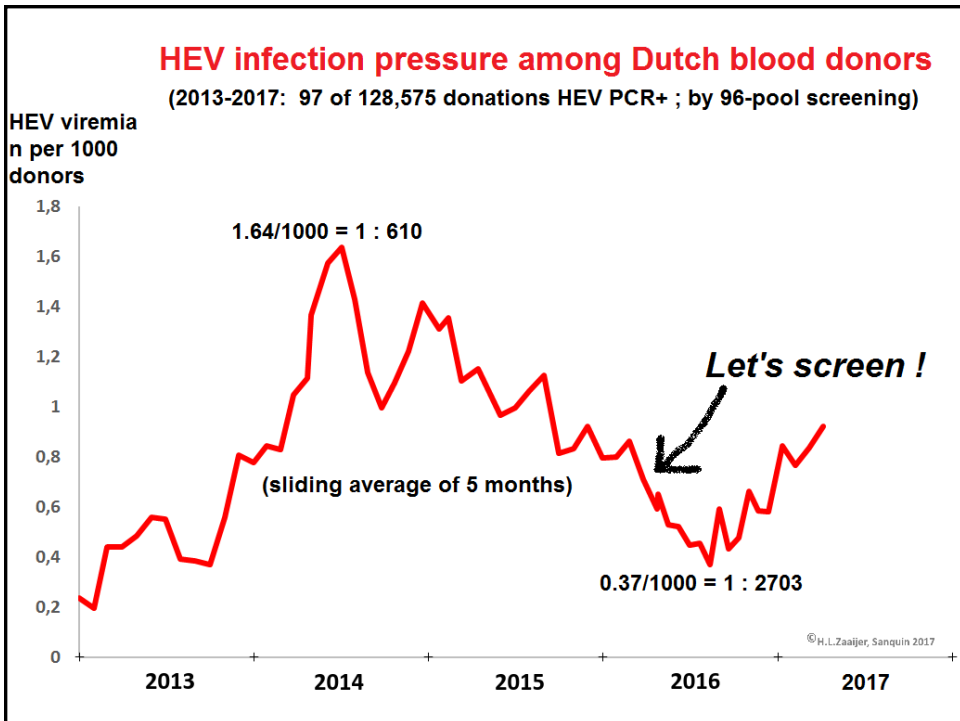
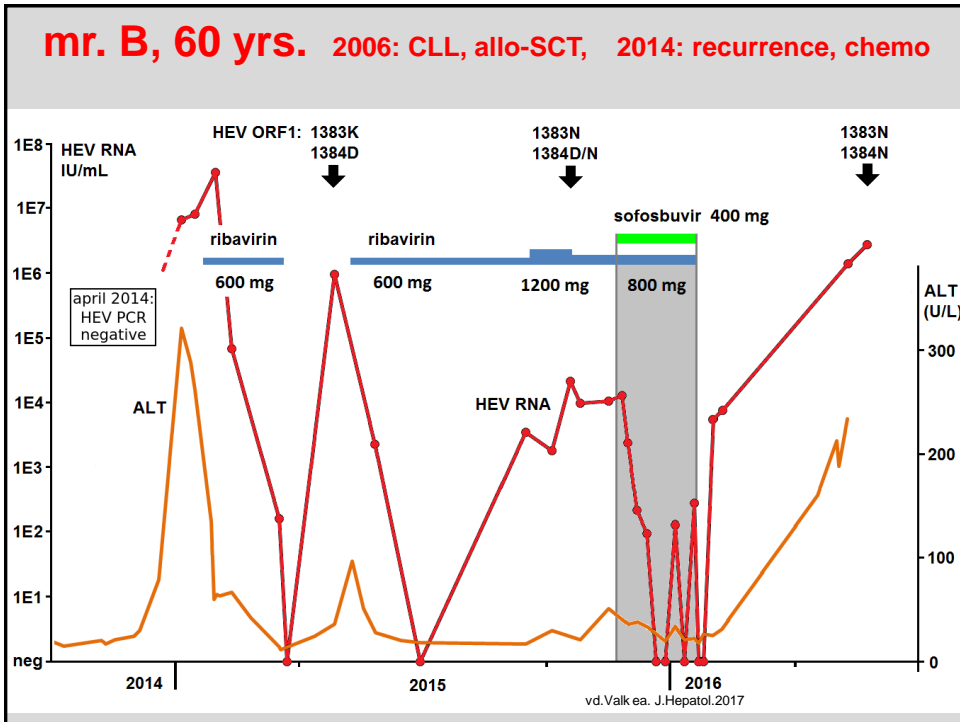
A. Bouts, *Pediatrics* 2015, vol 135, nr 4

step 1: tacrolimus to 5/6
 step 2: MMF to 3/4
 step 3: tacrolimus to 4/6
 step 4: tacrolimus to 3/6
 step 5: tacrolimus to 4/6

mr. C, 51 yrs



de Niet ea. *Neth. J. Med.* 2012; 70: 261-266



Conclusies

- HEV uitbraak bedreigt specifieke patiënten.
- Risicopatienten: HEV diagnostiek met PCR.
- Orgaan Tx: 'drug induced liver injury' (dili) = HEV ?!
- Stam cel Tx: 'graft versus host vd. lever' (incl.PA) = HEV ?!
- riba-kuur: pas stoppen als plasma en faeces 3 mnd PCR neg.

- Dit is 3^e zoönose vanuit onze bio-industrie; economisch belang prevaleert opnieuw.
- Overheid beveiligd alleen bloedtransfusie (donorscreening per 3-7-17) ; voedsel/varkens ongemoeid, geen relevante studie gestart.
- 1:700 HEV infecties in NL door bloedprodukt.

- HEV gt3 = oraal vaccin tegen HEV gt1/2 ?



Bloedoverdraagbare
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