

Hepatitis E virus *genotype 3* : what we know so far

May 20th, 2015

Hans L. Zaaijer MD PhD

Sanquin - Blood-borne Infections &

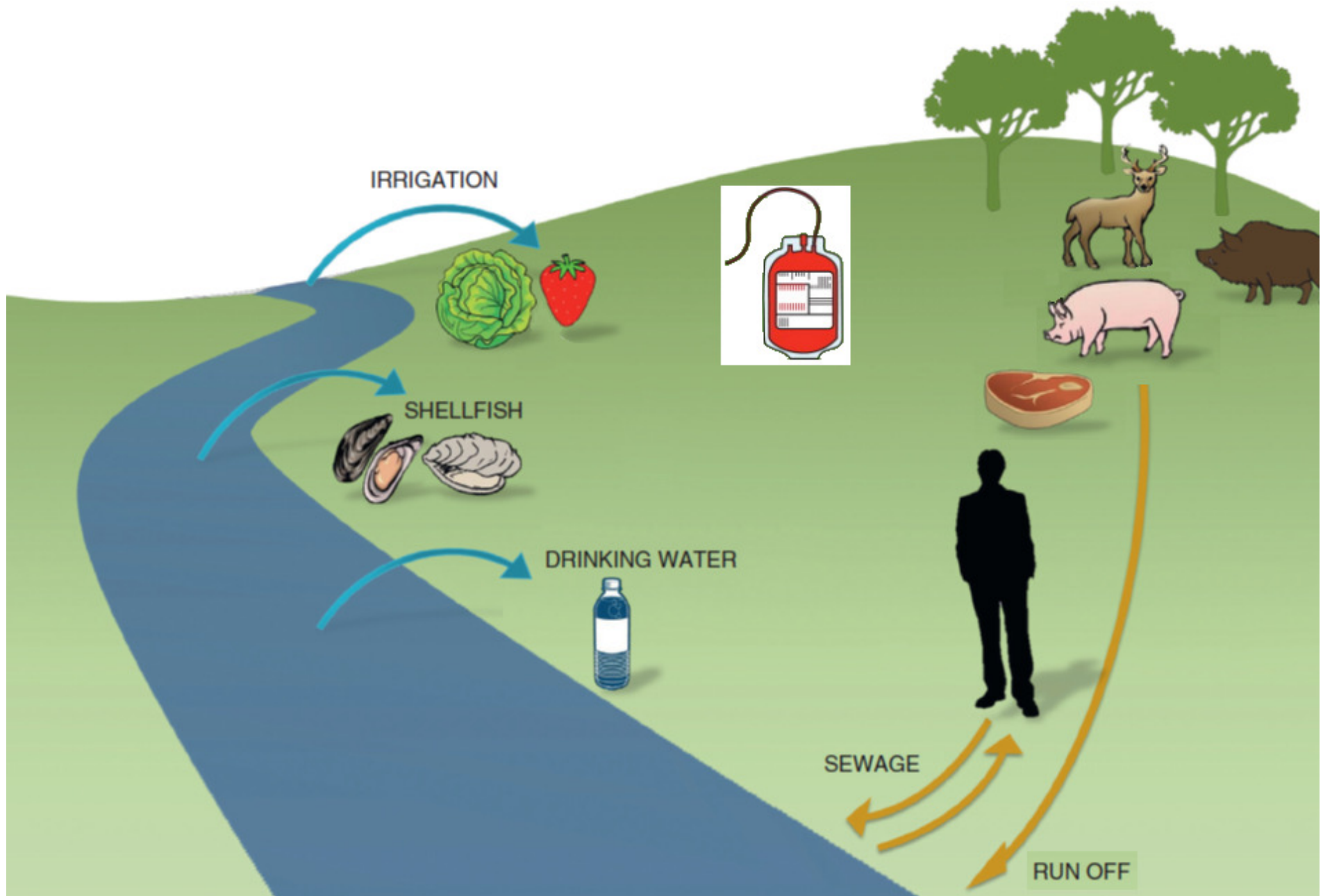
Academic Medical Centre - Clinical Virology

Amsterdam NL



HEV gt 3: the issues

- sources and routes of infection
- incidence and course of infection in blood donors
- infectivity, inactivation and removal of HEV gt3
- course of gt3 hepatitis E in patients
- consequences for blood safety



adapted from: WHM vd Poel - Current Opinion in Virology 2014, 4:91–96

sources and routes of infection

- pooled feces from 97 Dutch pig farms:
51/97 (53%) HEV RNA positive.

Rutjes ea, Em.Inf.Dis. 2009

- pork products in France:
figatelli 30%; liver sausages 29%; quenelles 25%;
dried salted liver 3% HEV RNA positive.

Pavio ea, Em.Inf.Dis. 2014

- pork products in UK:
consumption of pork pie, ham and sausages from major UK
supermarket chain signif. associated with indigenous infection.

Said ea, Epid.Inf. 2013

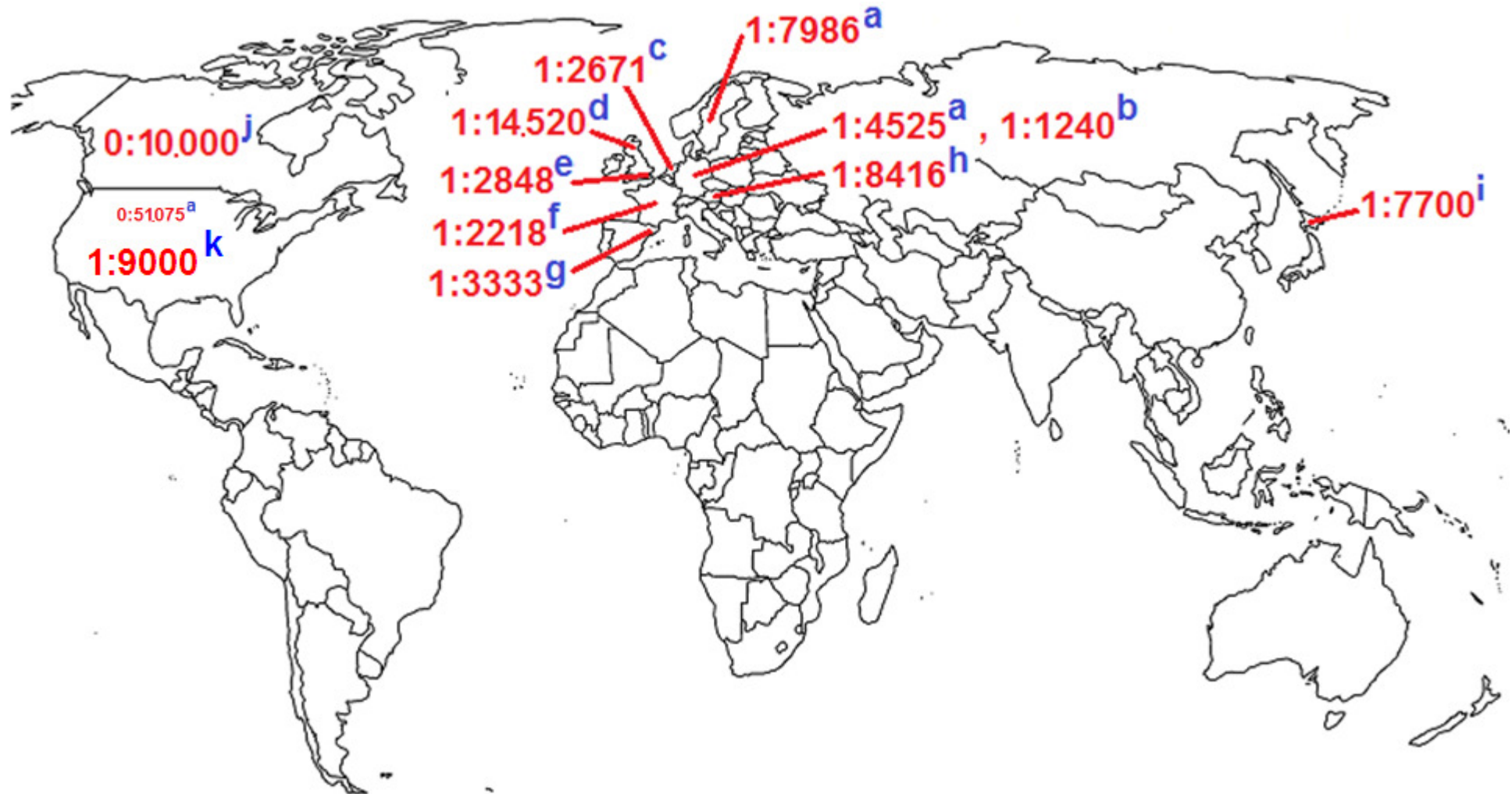
- leafy green vegetables in Serbia, Greece, Poland:
5/146 (3.4%) samples HEV RNA positive.

Kokkinos ea, Food Env.Vir. 2012

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HEV RNA positive blood donors

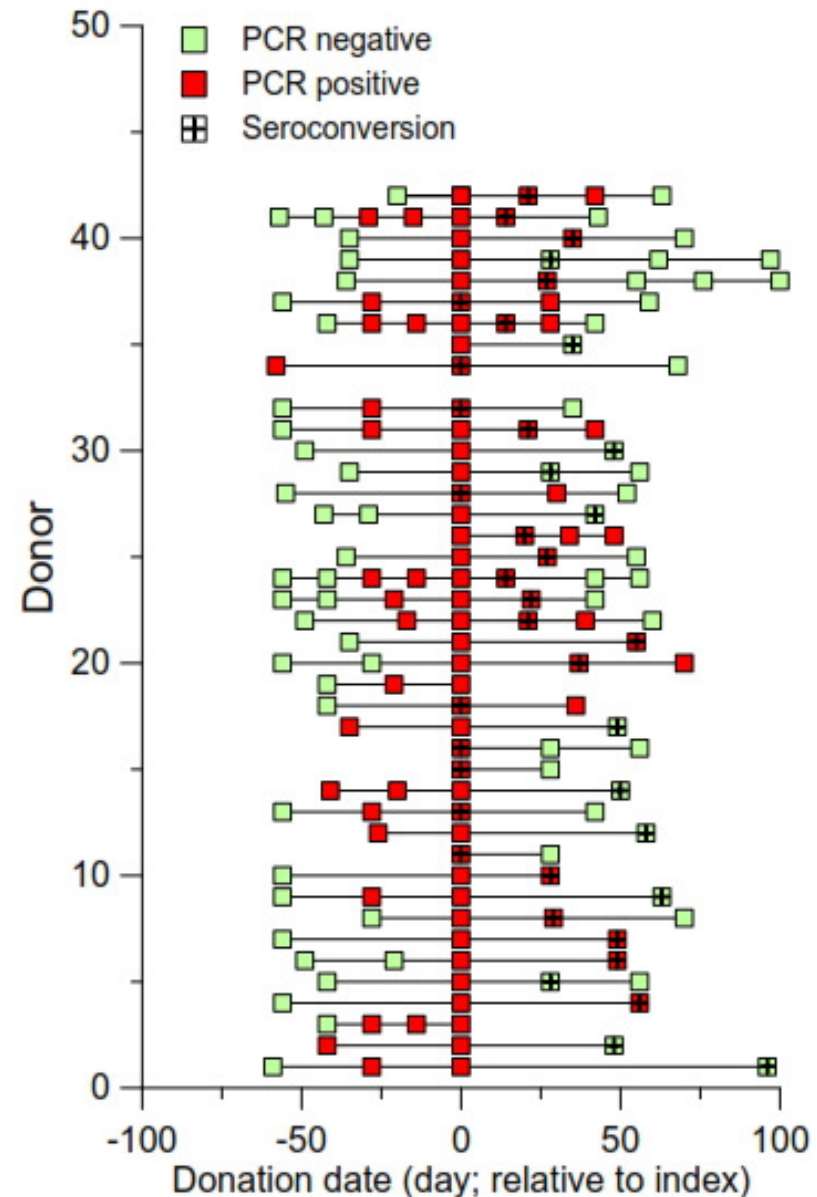


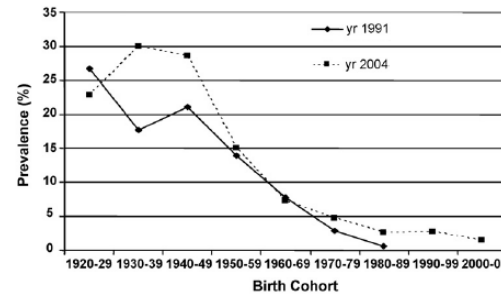
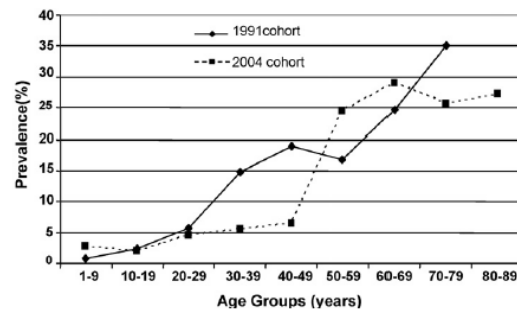
a) Baylis, Vox 2012; b) Vollmer, JCM 2012; c) Slot, EuroSurv.2013; d) Cleland, Vox 2013;
e) Hewitt, Lancet 2014; f) Gallian, EID 2014; g) Saulea, Transfusion 2014; h) Fischer, PlosOne 2015;
i) Ikeda, ISS 2009; j) CBS Surveillance Report 2014; k) pers. communication J.S. Epstein.

Course of infection in 41 NL blood donors

presentation by dr. Hogema:

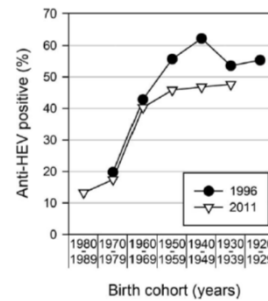
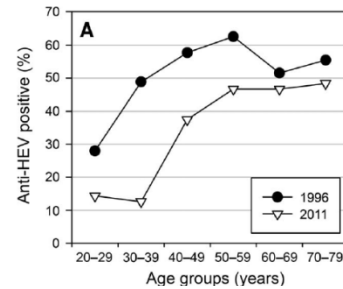
- duration of viremia.
- 2/3 seroneg. : seroconverted
- serial viremic donations:
donors apparently not affected
- normal or slightly elevated ALT
(several reports)
- does viremic re-infection occur?



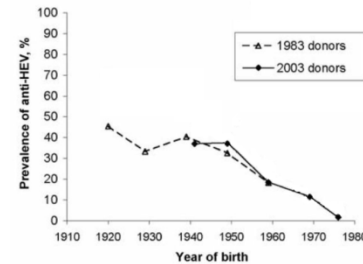
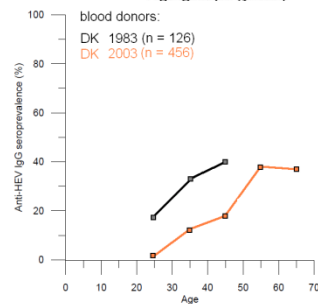


anti-HEV seroprevalence: age cohort effect

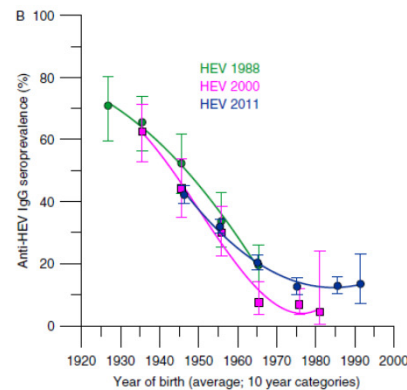
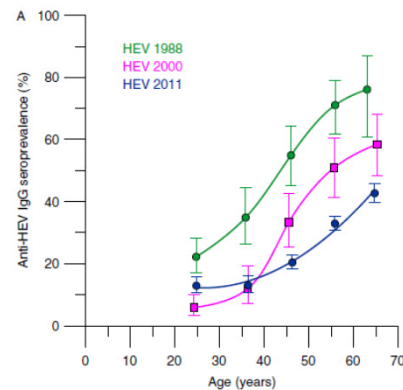
Ijaz ea (UK),
JCV 2009



Wenzel ea (SE.Germany),
Hepatol. 2014



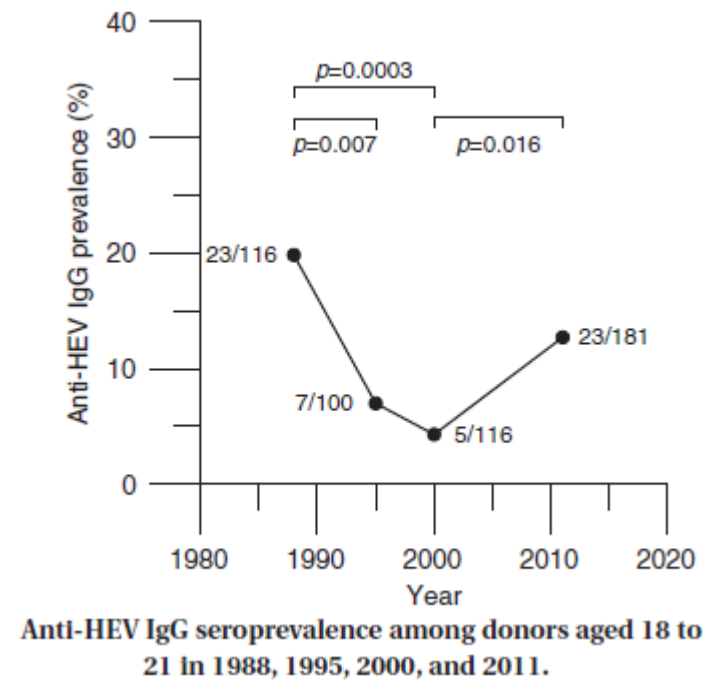
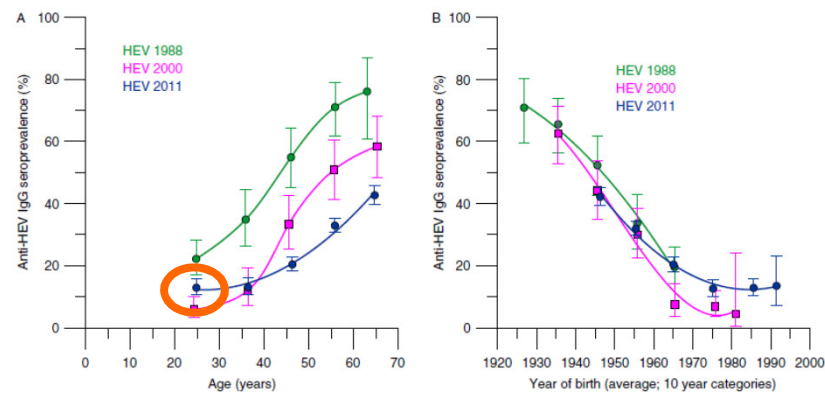
Christensen ea (Denmark),
CID 2008



Hogema ea (NL),
Transfusion 2014

anti-HEV seroprevalence: age cohort effect

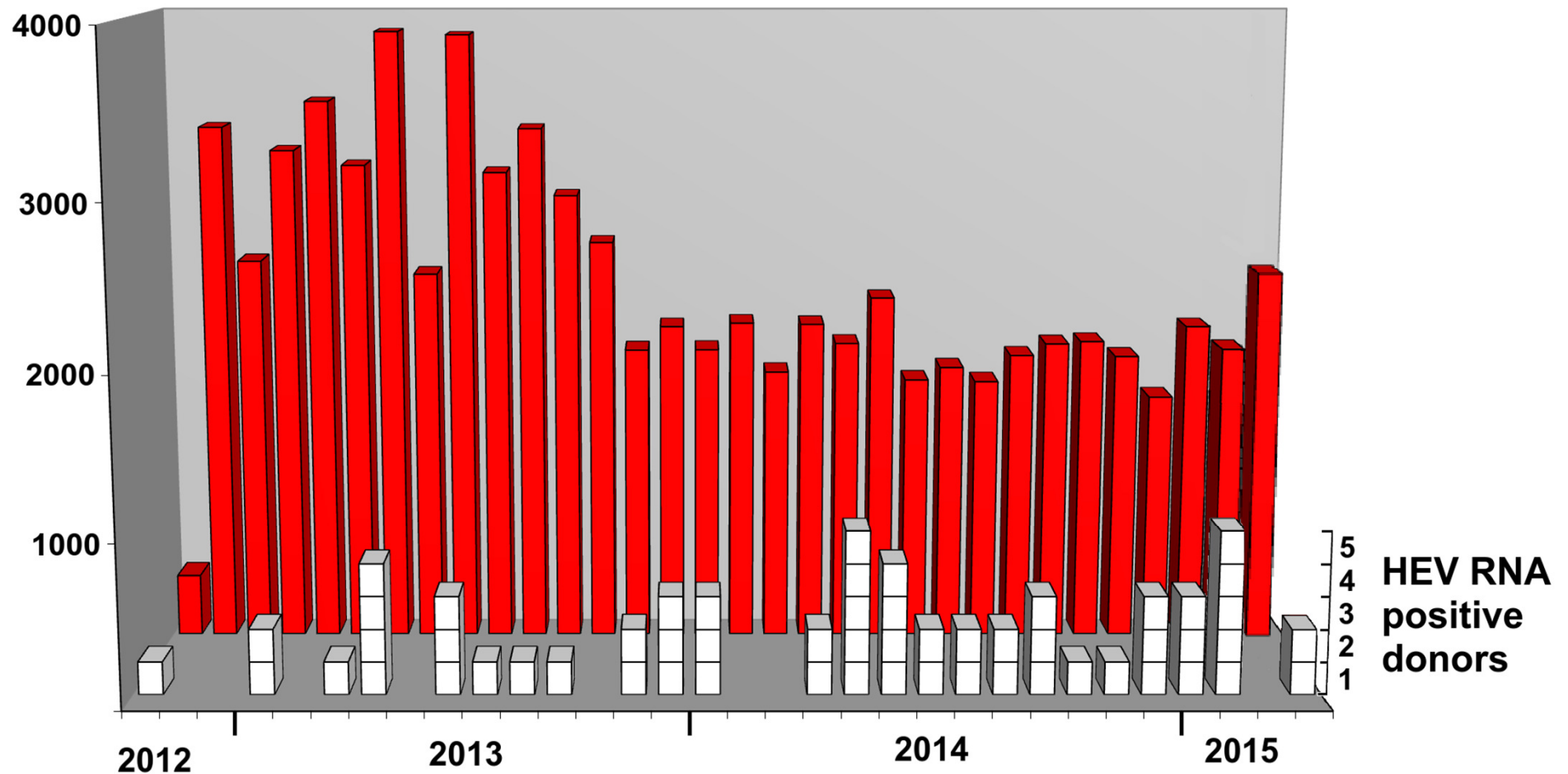
and recent increase of
incidence:



Monthly donorscreening for HEV RNA in NL

~2000 donations/month; in pools of 96; for SD-plasma production

Dutch donations screened for HEV RNA



© Hans Zaaijer, Sanquin 2015

overall: 57 / 73341 (1:1287) donations HEV+ (all asymptomatic, 'acute': seroconverting)

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

Lancet, 2014

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

Serological and molecular evidence of a plausible transmission of hepatitis E virus through pooled plasma

Vox, 2014

A. Andonov,¹ G. Rock,² L. Lin,¹ J. Borlang,¹ J. Hooper,¹ E. Grudeski,¹ J. Wu³ & Members of the Canadian Apheresis Group

Hepatitis E transmission by transfusion of Intercept blood system–treated plasma

Hauser ea (France)

Blood 2014

TRANSFUSION-TRANSMITTED HEPATITIS E IN GERMANY, 2013

Eurosurv. 2014

D Huzly, M Umhau, D Bettinger, T Cathomen, F Emmerich, P Hasselblatt, H Hengel, R Herzog, O Kappert, S Maassen, E Schorb, C Schulz-Huotari, R Thimme, R Unmüßig, J J Wenzel, M Panning

Transfusion-transmitted hepatitis E in a patient with myelodysplastic syndromes

Blood Transf. 2014

Yukihiko Kimura¹, Akihiko Gotoh², Seiichiro Katagiri², Yuji Hoshi⁴, Shigeharu Uchida⁴, Atsushi Yamasaki⁵, Yoko Takahashi³, Katsuyuki Fukutake³, Toru Kiguchi⁶, Kazuma Ohyashiki²

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2012-2013: 79 / 225,000 donations (1:2848) HEV+ (all gt3):

- 18/43 (42%) of recipients infected
- transmission associated with: viral load, seronegative donor.

> Not all viremic donors transmit HEV.

Cave pseudo transmission:

11 cases of “post-transfusion hep E” notified to Sanquin:

10 : all implicated donations HEV PCR negative.

1 : 1 implicated donor HEV RNA positive.

HEV: inactivation and removal

ad interim interpretation at Sanquin:

Effective removal or inactivation:

- Planova15N or Planova20N filtration
- Pasteurisation at 60 °C
- Immunoaffinity chromatography purification

Limited or no inactivation:

- SD treatment
- Low-pH treatment
- Alcohol fractionation
- Neutralisation by anti-HEV antibodies

(due to a protective lipid layer covering HEV virions in blood:
only neutralisation in serum or cell cultures after SD- or protease treatment)

See:

Summary of workshop presentations in Appendix to reflection paper, of the “EMA Workshop on viral safety of plasma-derived medicinal products with respect to hepatitis E virus” (London, Oct. 28th/29th, 2014); aimed to be released for public consultation in July 2015.

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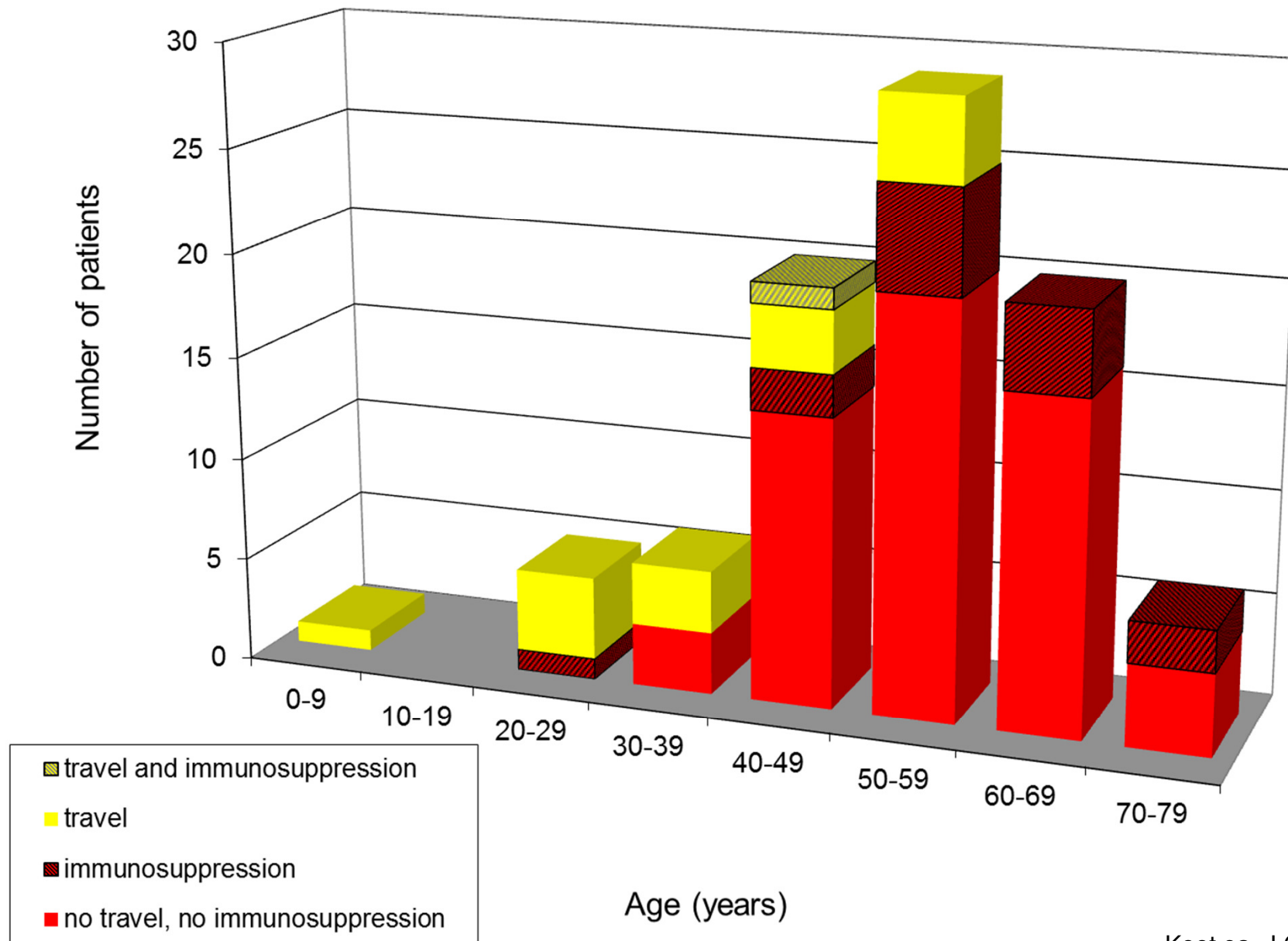
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course of HEV gt3 infection in patients

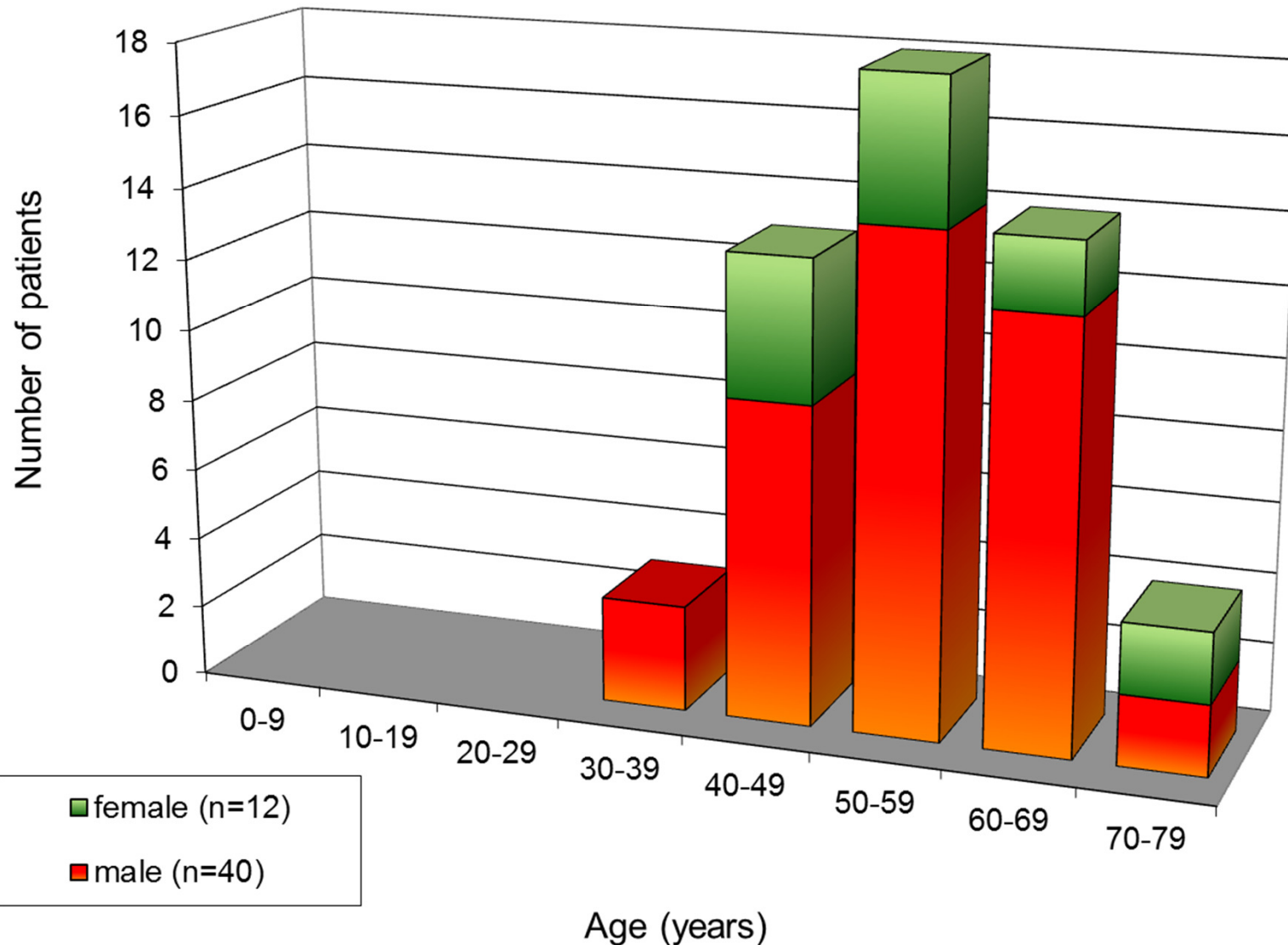
1. the good news about HEV gt3:
apparently no morbidity in pregnant women,
newborns, children and majority of adults
2. acute, mild hepatitis in middle aged (wo)men :

81 Dutch hep. E patients: risk factors

2009-2014: 4067 samples submitted for 'hep.serology' : 144 HEV-IgM and PCR pos. > questionnaire > 81 responses



**subset: 52 Dutch hep E patients,
no travel and no immune sup./def.**



course of HEV gt3 infection in patients

1. the good news:

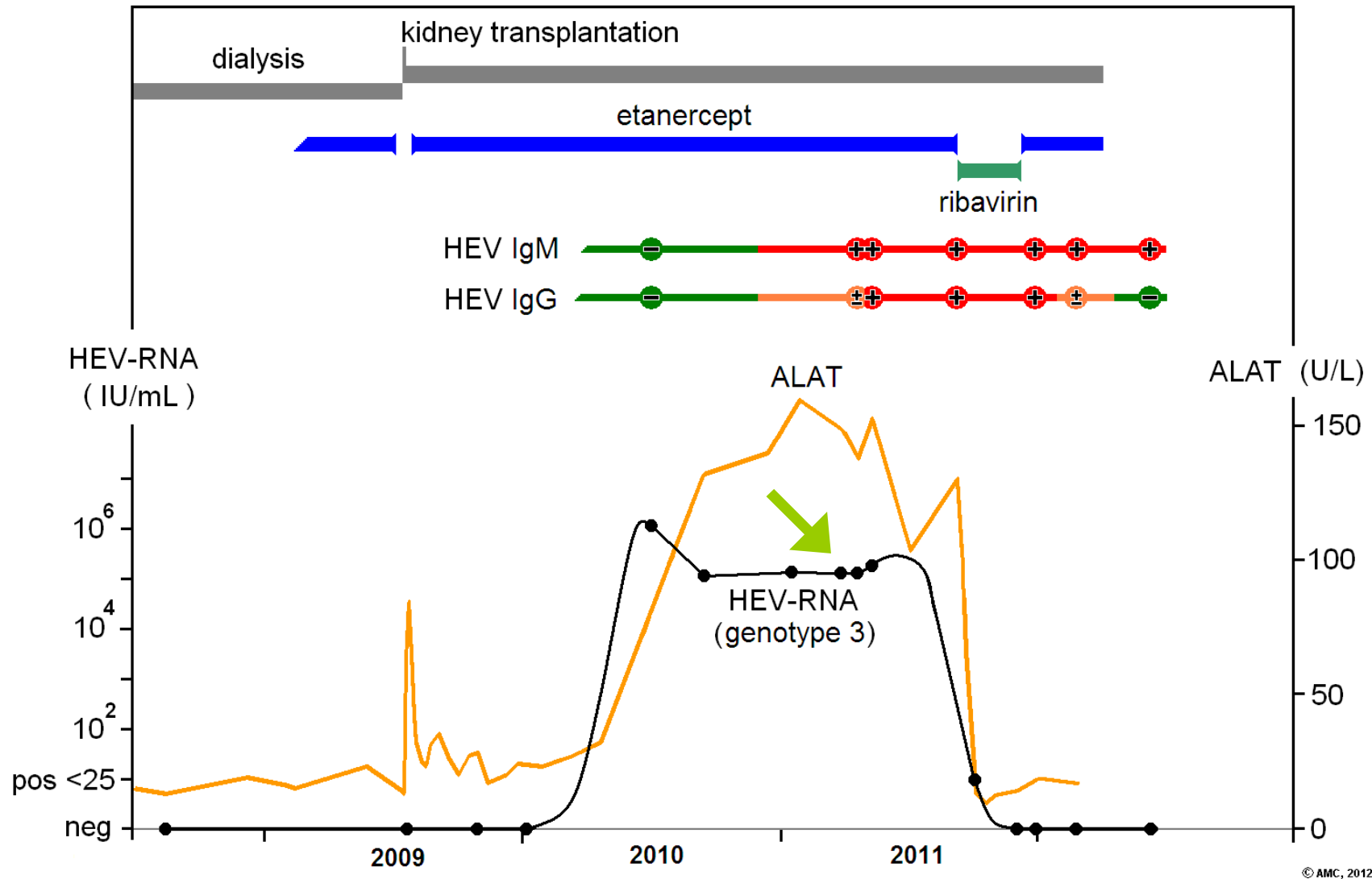
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2. acute, mild hepatitis in middle aged (wo)men

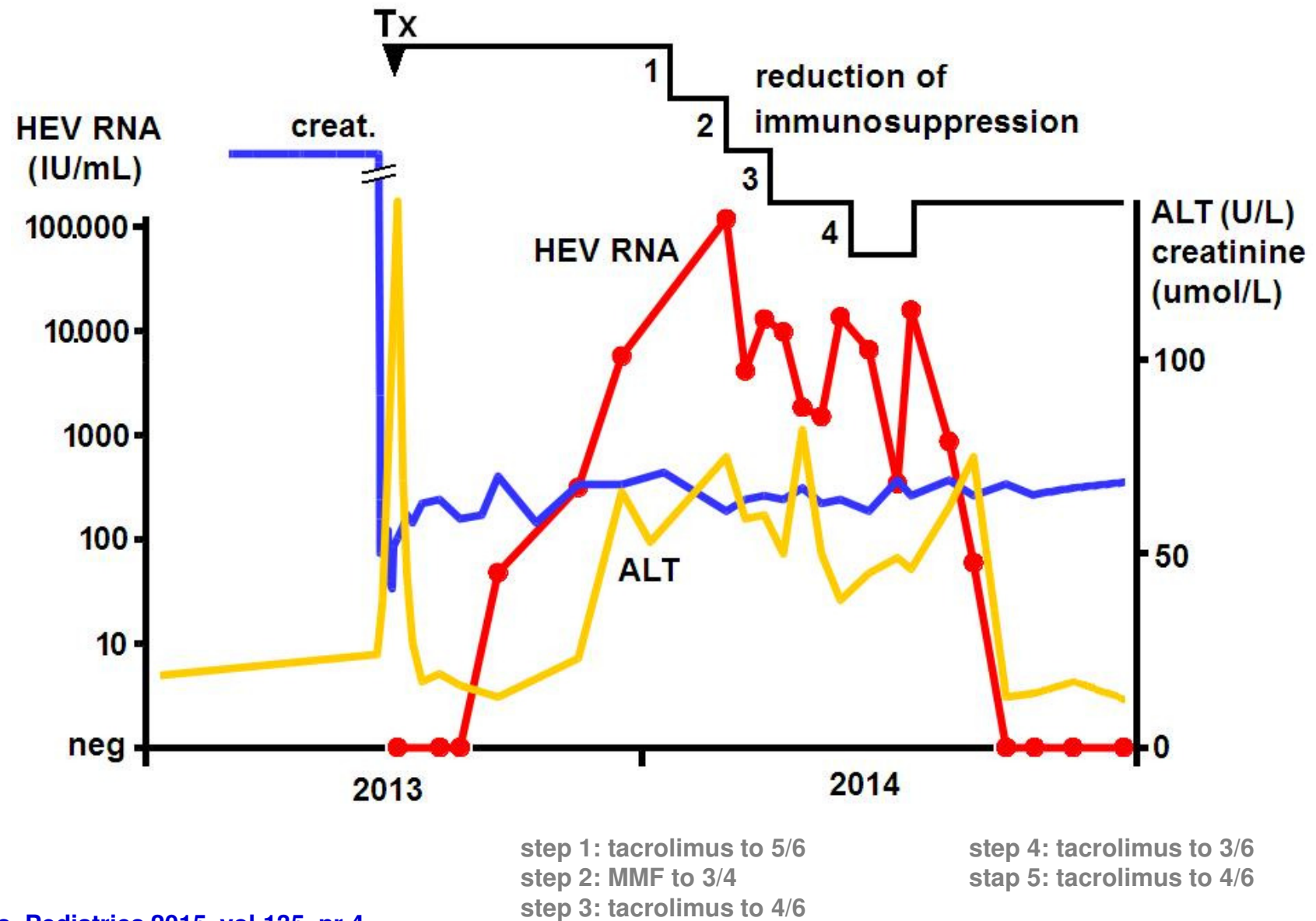
3. acute and/or chronic hepatitis in transplant, chemo, etc. patients:

- mimicking drug induced liver injury
- mimicking graft versus host disease of the liver
- *rapid cirrhosis*

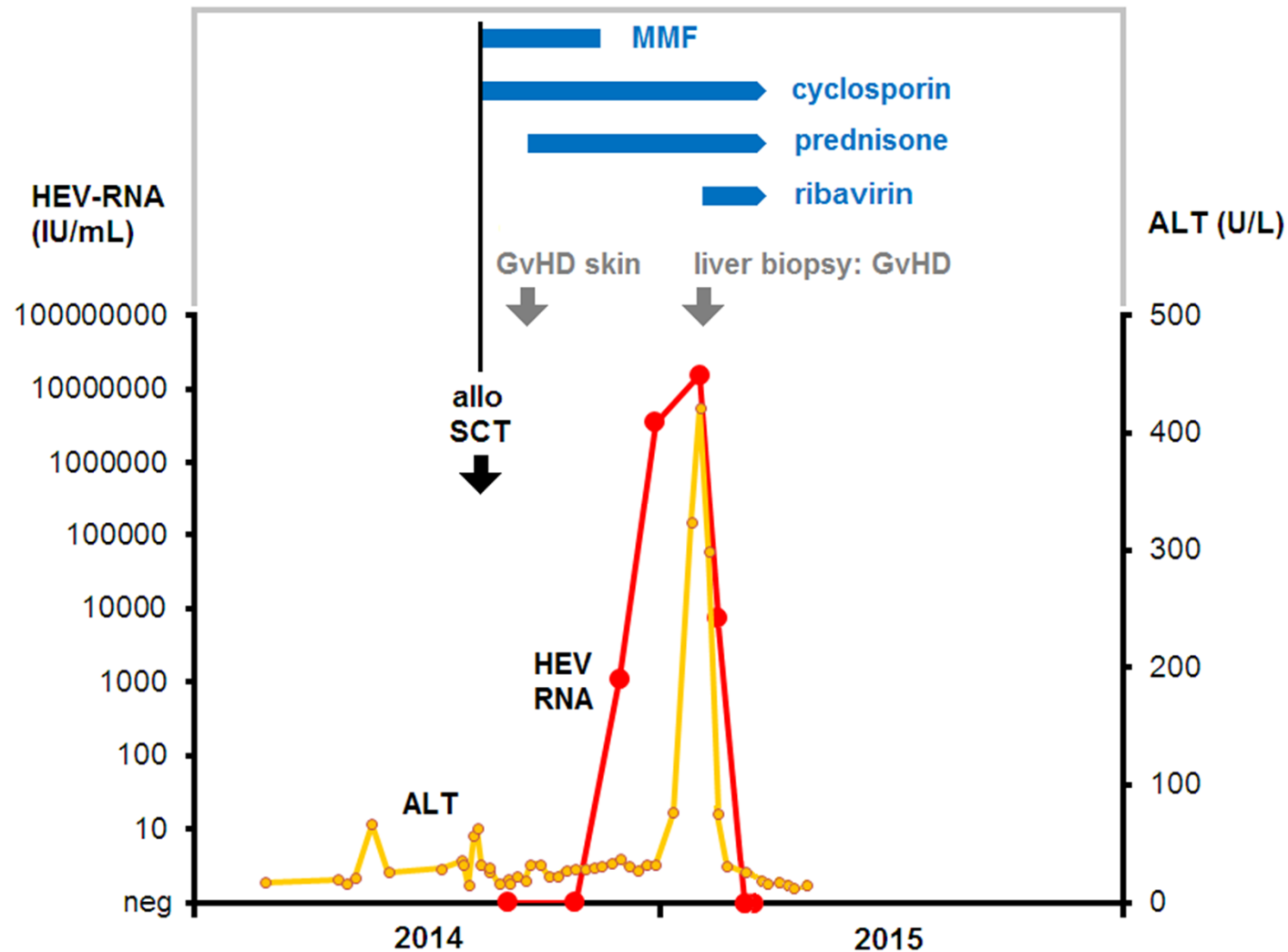
case 1: mr. A, 51 yrs



case 2: girl B, 11 yrs kidney failure e.c.i.



case 3: mrs. C, 55 yrs



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HEV gt3 and blood banking

General considerations:

- HEV gt3 poses a threat to immunosuppressed patients, but timely diagnosis and treatment are possible.
- Vulnerable patients must be screened for HEV, irrespective of blood transfusion/products. (Based on ALT elevation, or once a year?)

Options for donor screening:

- none / for at-risk recipients / universal.
- If donor screening is indicated: above which incidence?
- pooled or individual HEV NAT? Or are HEV IgG+ donors safe (NL: 27%) ?
- Sanquin: “Make food and water safe, in stead of blood supply”.

Policy and decision making:

UK: SaBTO HEV Blood Services Sub Group is studying options.

NL: Ministry of health has to answer 20+ HEV related questions posed by members of parliament.

France, Germany, Spain, Japan, Ireland:

HEV team at Sanquin:

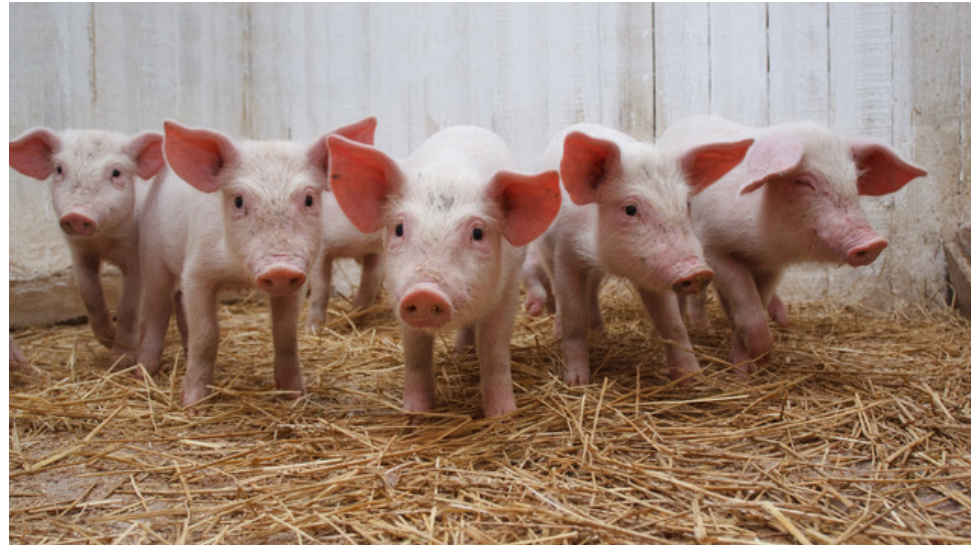
Boris Hogema

Michel Molier

Ed Slot

Hidde Koot

Hans Zaaijer



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