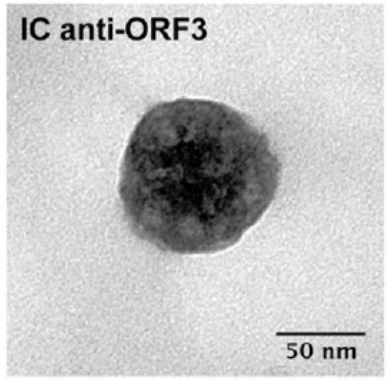
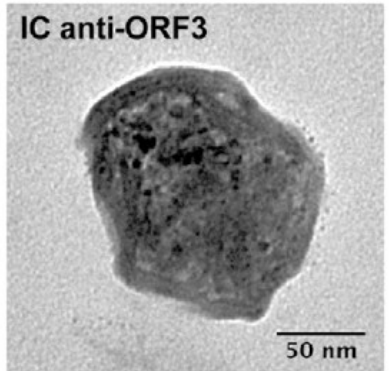


serum



stools

HEV

Introduction, Virological aspects

Professor Françoise Lunel Fabiani, Virology Laboratory, CHU Angers, France

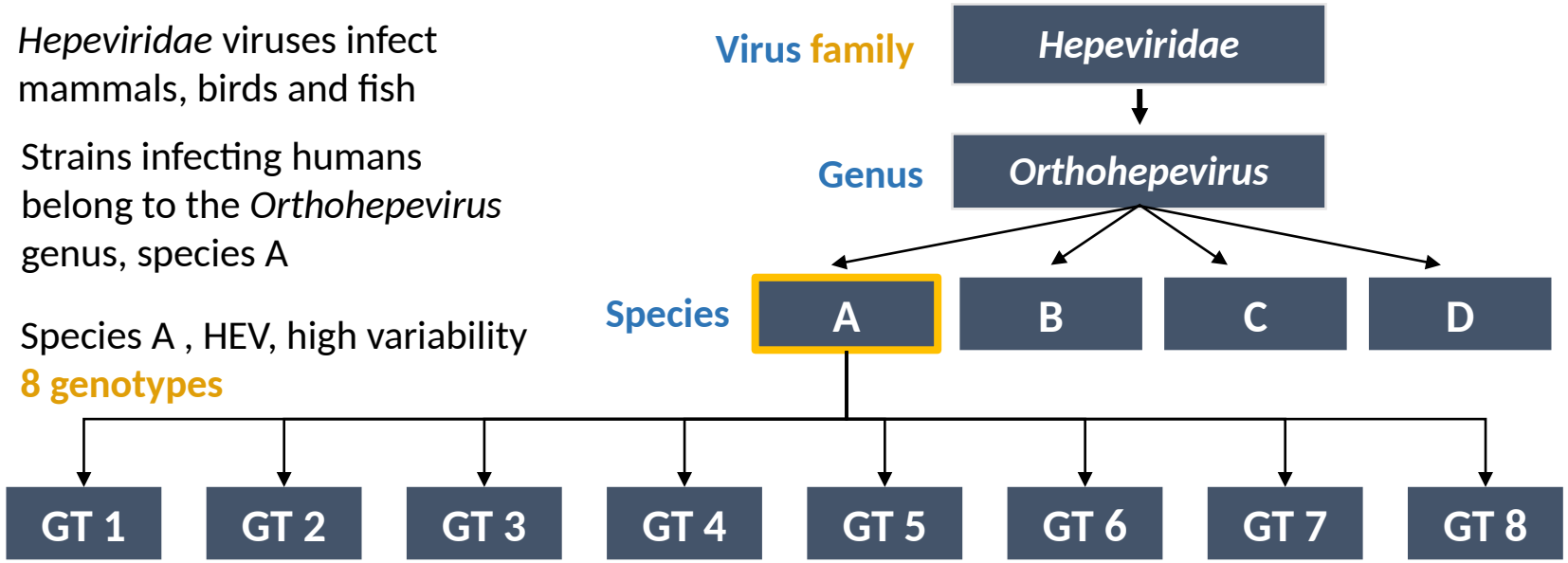
Virology

HEV : 30 to 34 nm RNA non enveloped virus

Hepeviridae viruses infect mammals, birds and fish

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

Species A , HEV, high variability
8 genotypes



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

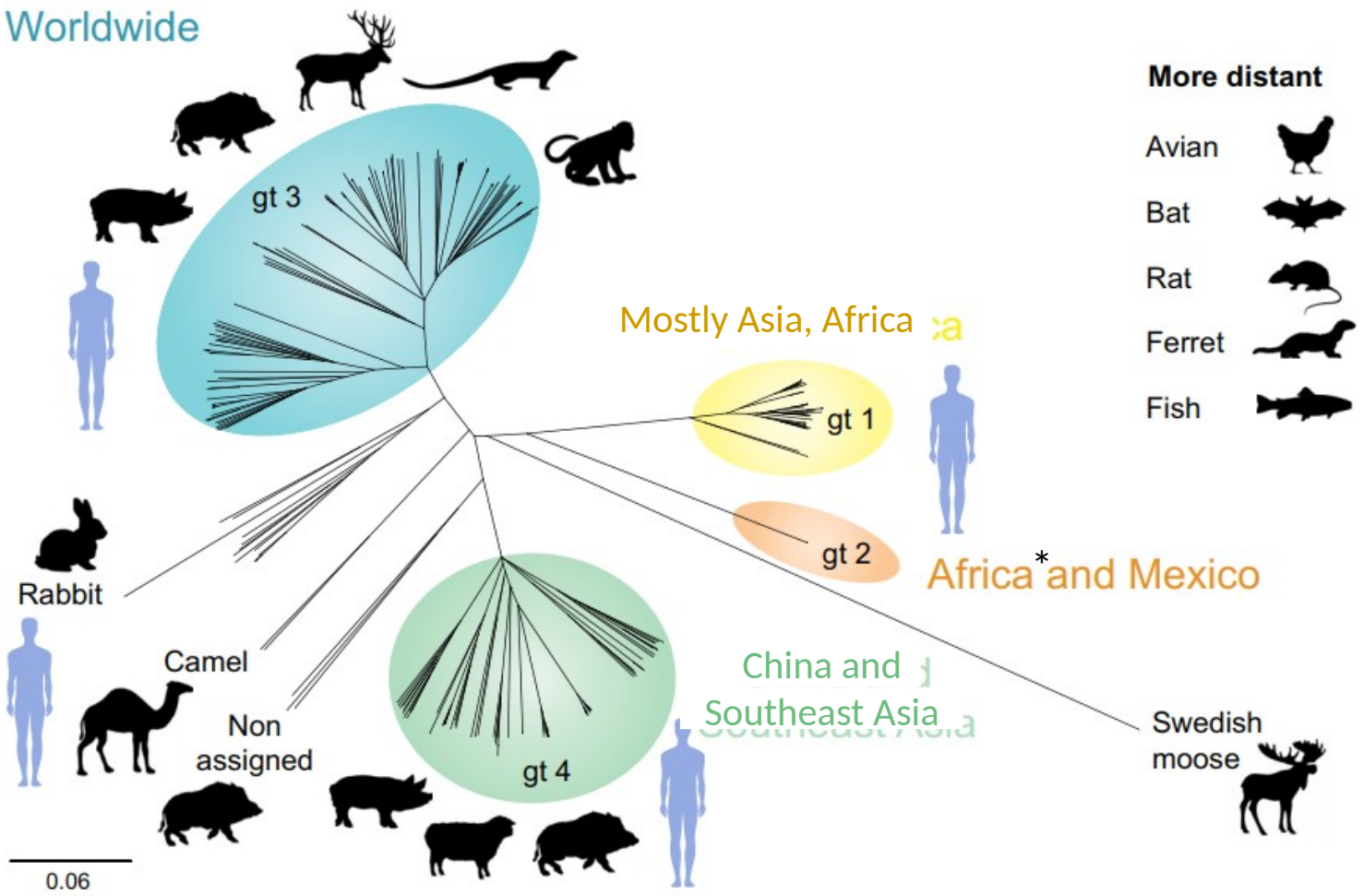
- **Endemic** in animal species; eg, pigs and wild boar
- **Zoonotic** infections in humans
- **High-income countries**
- China: GT 4 most common
- S. America: GT 3 only

- Have only been reported in wild boar

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

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

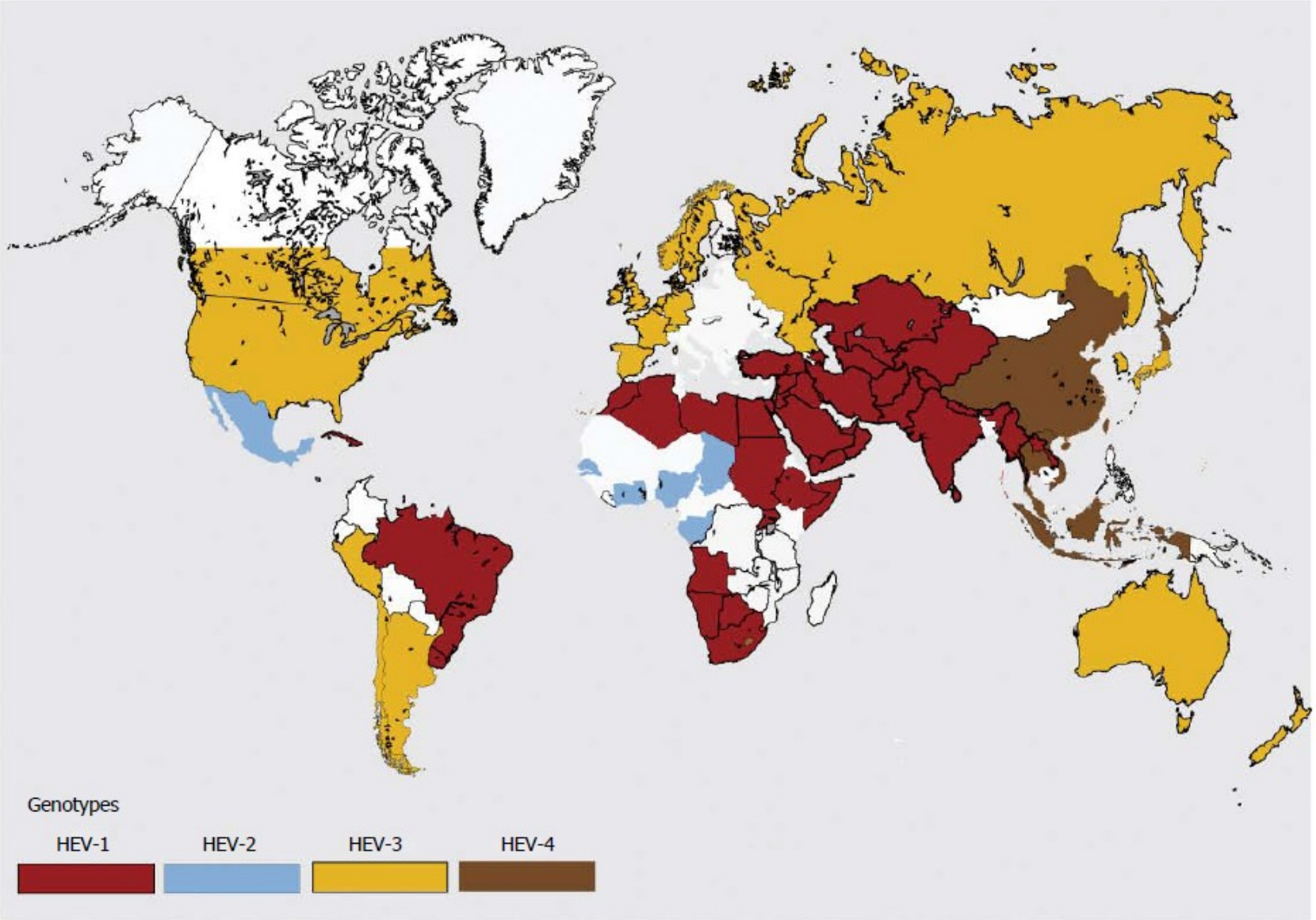
Phylogenetic relationship of hepeviruses



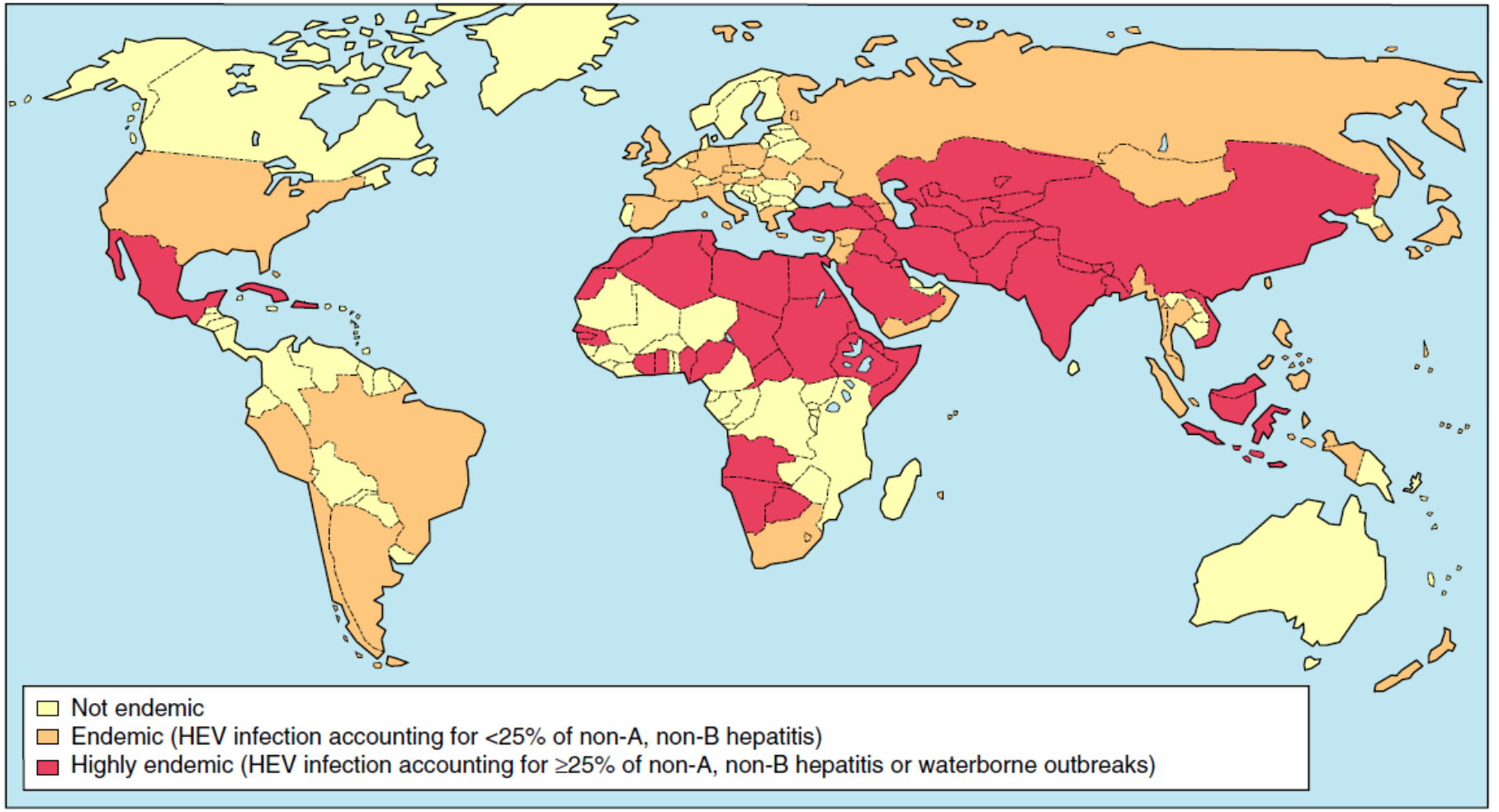
* Namibia and Nigeria

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

Geographical distribution of HEV genotypes, *Khuro et al, WJG 2016*



HEV(G1 G2) 1st cause of acute hepatitis around the world



Donnelly et al, APT 2017

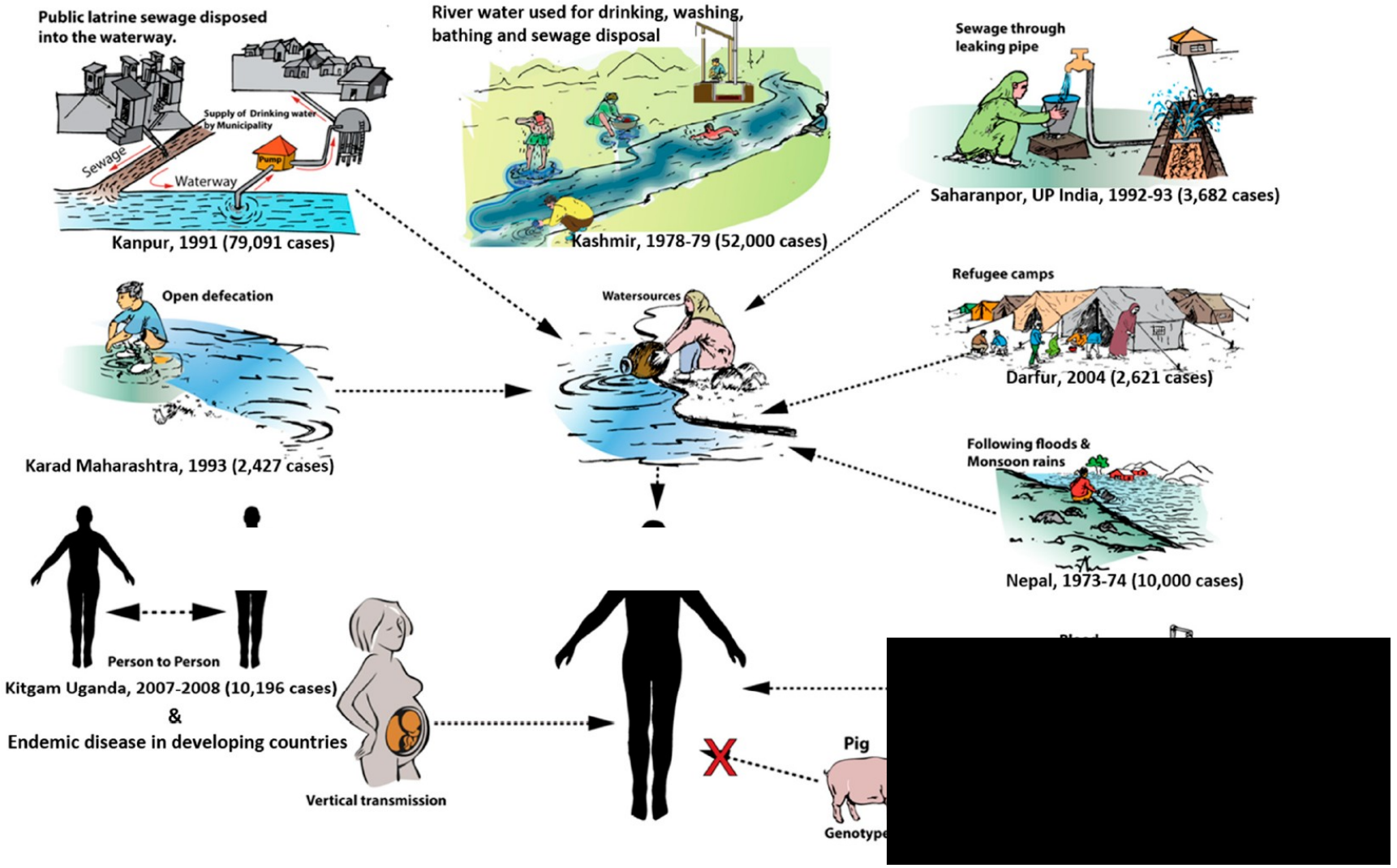


Figure 2. Modes of transmission of hepatitis E in developing countries. The settings for contamination of drinking water have been drawn in sketches, with epidemics reported in each case.

HEV genotype 1 and 2 – in developing countries - mode of transmission

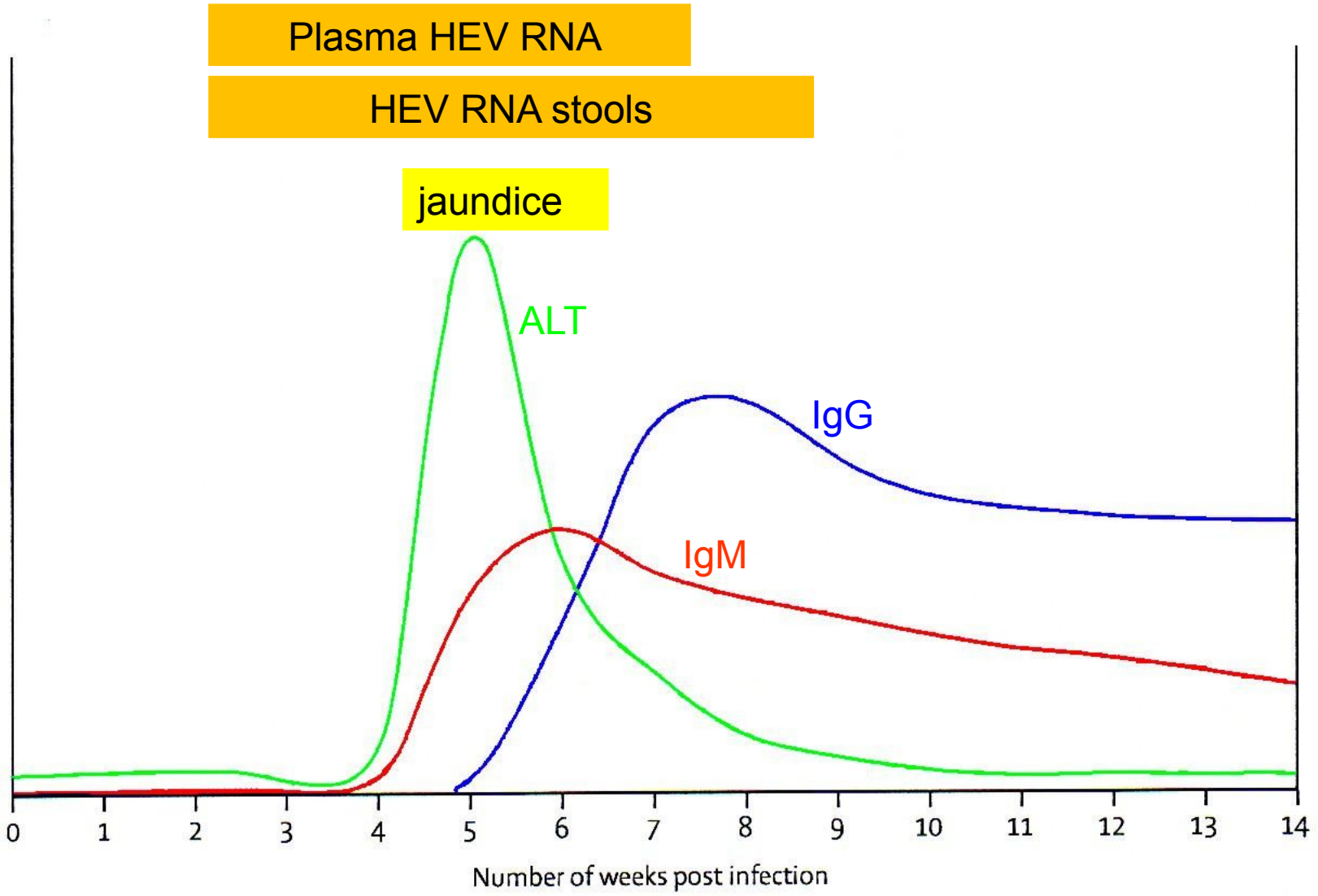
HEV GT 3 and 4*: epidemiology

- Endemic in some developing countries, as well as most high-income countries
- Most common cause of acute viral hepatitis in many European countries
- Estimated that ≥2 million locally acquired HEV infections/year
  - Most as a result of zoonotic infection
    - Primary hosts are pigs
- HEV GT 3 and 4 tend to affect older males
  - Incidence varies between and within countries, and over time
  - Multiple 'hotspots' of HEV infection in Europe

* China and Taiwan

1. Dalton HR, et al. Eur J Gastroenterol Hepatol 2008;20:784–90;
EASL CPG HEV. J Hepatol 2018;doi: 10.1016/j.jhep.2018.03.005 [Epub ahead of print]

Natural History- HEV Diagnosis



Kamar, Clin Microb Rev, 2014

New tests

✓ **VIDAS ® IgG et IgM anti-HEV, Biomérieux**

➔ **Sensitivity IgG 0,56 U/ml**

		Infectious profile			
		Viremic phase	Post-viremic phase	No recent infection	Total
VIDAS®	**Positif**	83	42	2	127
Anti-HEV IgM	**Négatif**	2	29	301	332
Total		85	71	303	459
Performances		%	[IC95%]		
Positive concordance for viremic phase (acute phase)		**97.65 %**	[91.76 ; 99.71] %		
Positive concordance for post-viremic phase		***59.15 %***	[47.54 ; 69.83] %		
Negative concordance		**99.34 %**	[97.64 ; 99.92] %		

Abravanel, ESCV 2017

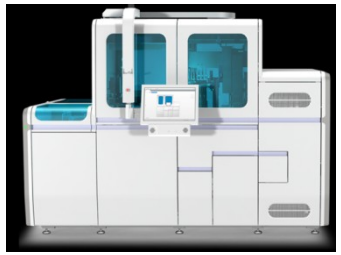
✓ **VIRCLIA ® / ALEGRIA ® IgG et IgM anti-HEV, Orgentec**

Performance ???

Direct Tests

✓ **HEV RNA: PCR ou TMA, LoD 10-60 UI/ml**

Abravanel, *J Clin Microbiol* 2013 ; Gallian, *Transfusion* 2017



Cobas 6800
Roche ®

Procleix Grifols ®,
Panther Hologic ®

Real Star HEV V2 Altona®

Qualititatives

Quantitative

✓ **HEV Ag**

specificity : 100 %

diagnostic sensitivity : 91 %

80 % immunocompetent

94 % l'immunosupressed

analytic sensitivity < PCR or TMA

Wen, *J Clin Microbiol* 2015 ; Trémeaux, *J Clin Virol* 2016 ; Behrendt, *J Infect Dis* 2016

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
- Molecular tests are needed to diagnose or confirm infection, especially in immunosuppressed patients

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

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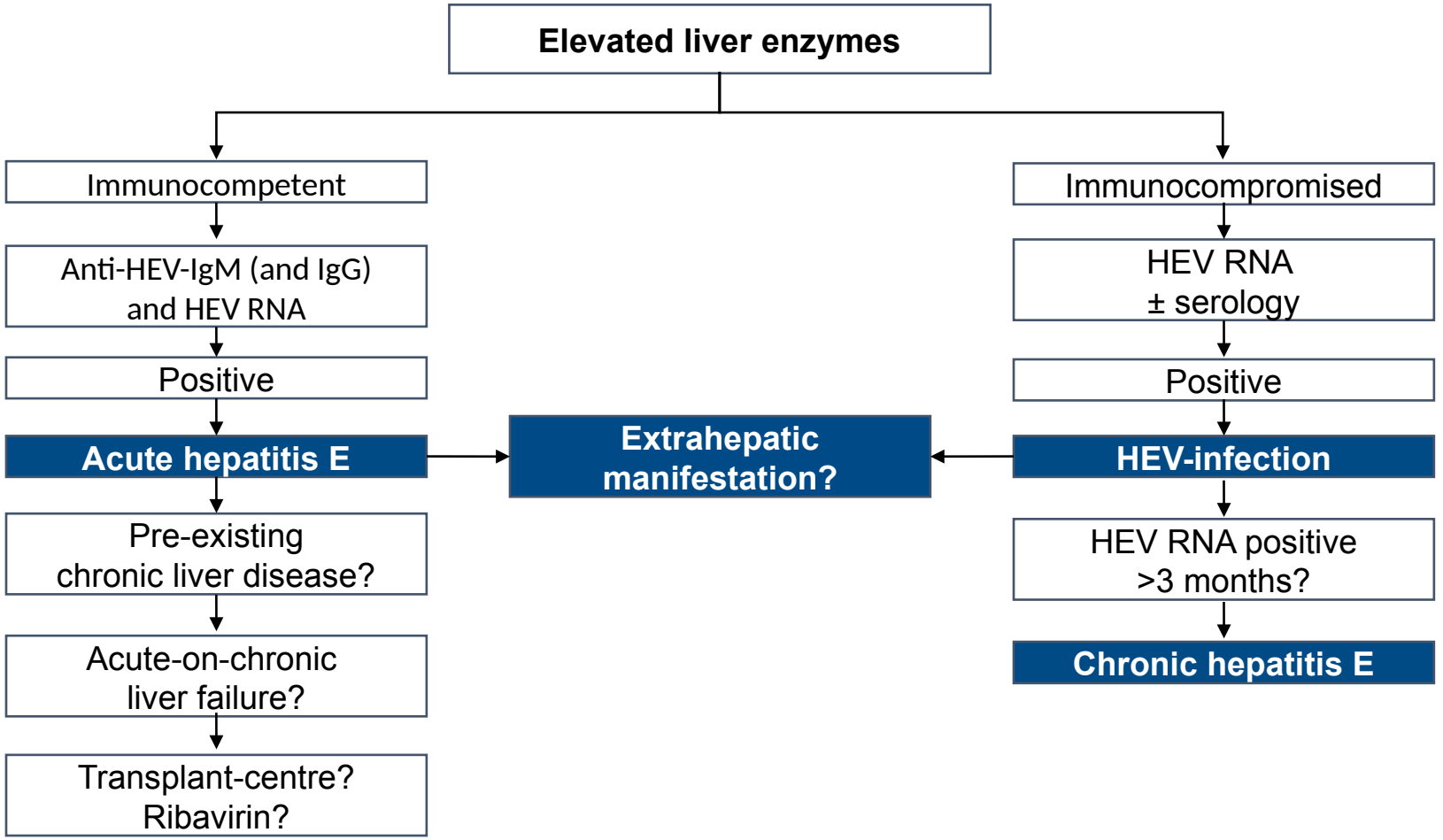
Diagnostic algorithm



Serology and NAT testing are best used in combination, as a negative PCR does not exclude acute infection; serology is sometimes negative in immunosuppressed patients with chronic infection

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