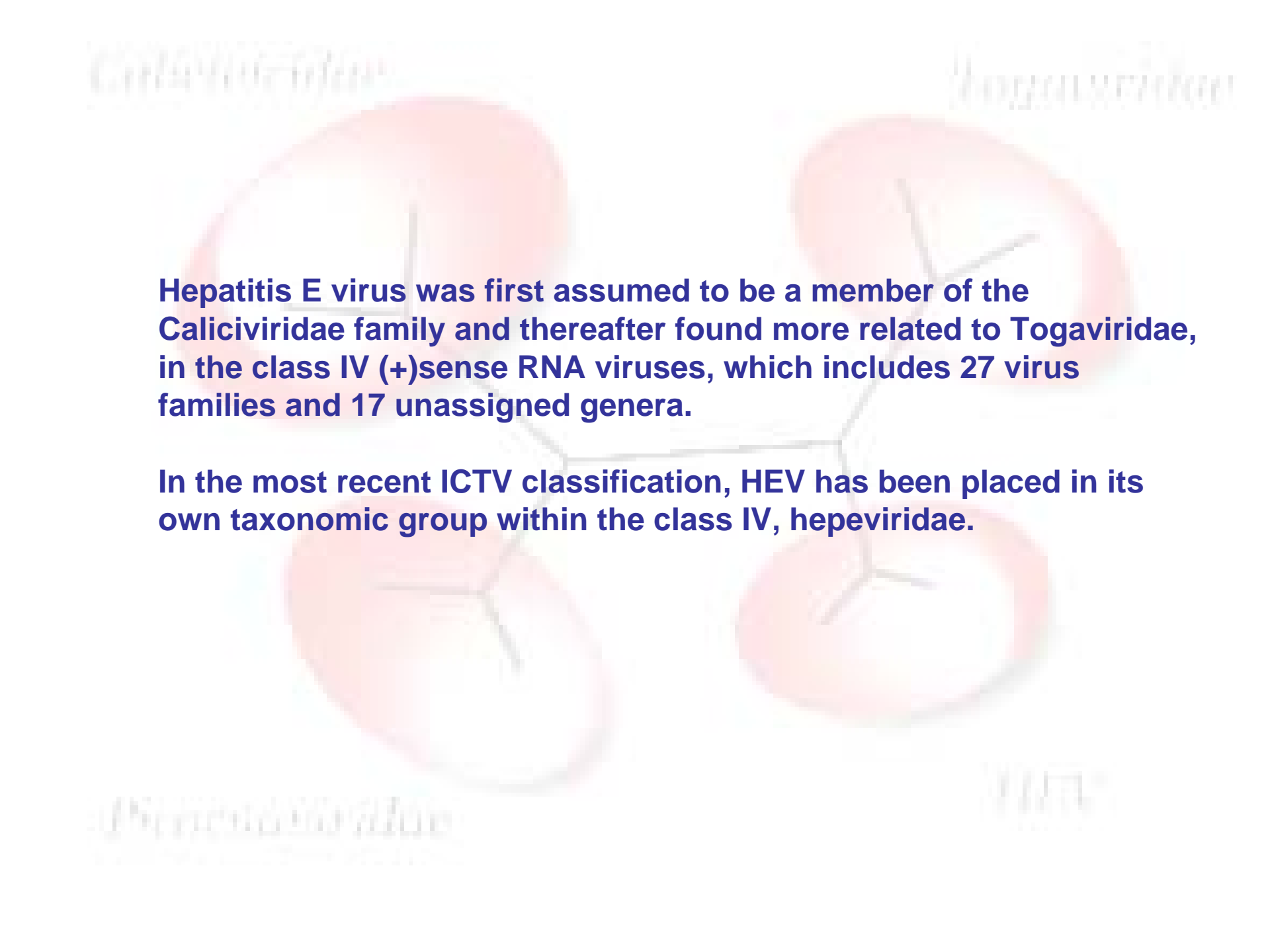


Molecular epidemiology and taxonomy of hepatitis E

Heléne Norder,
Swedish Institute for
Infectious Disease Control

Wang et al., 2008

journals.iucr.org/.../04/00/isscontsbdy.html



Hepatitis E virus was first assumed to be a member of the Caliciviridae family and thereafter found more related to Togaviridae, in the class IV (+)sense RNA viruses, which includes 27 virus families and 17 unassigned genera.

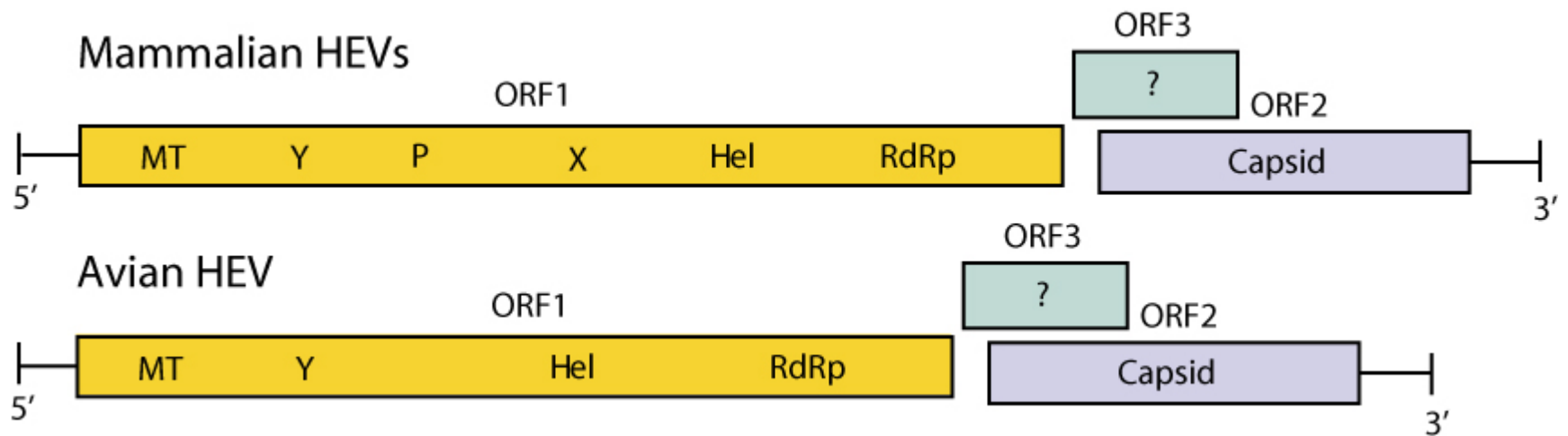
In the most recent ICTV classification, HEV has been placed in its own taxonomic group within the class IV, hepeviridae.

Hepatitis A

Hepatitis E

Virus family	picornaviridae	hepeviridae
Nucleic acid	plus strand RNA	plus strand RNA
Genomic size	7.5 kb	7.5 kb
Transmission	feces/(blood)	feces/(blood)
Incubation	2-5 weeks	3-7 weeks
Chronicity	none	not common (kidney transplant patients)
Mortality	1-2%	<1%, but 15-25 % in pregnant females
Severity of disease	increases with age	increases with age
Vaccine available	Yes	Yes, under development

Genomic organization of HEV

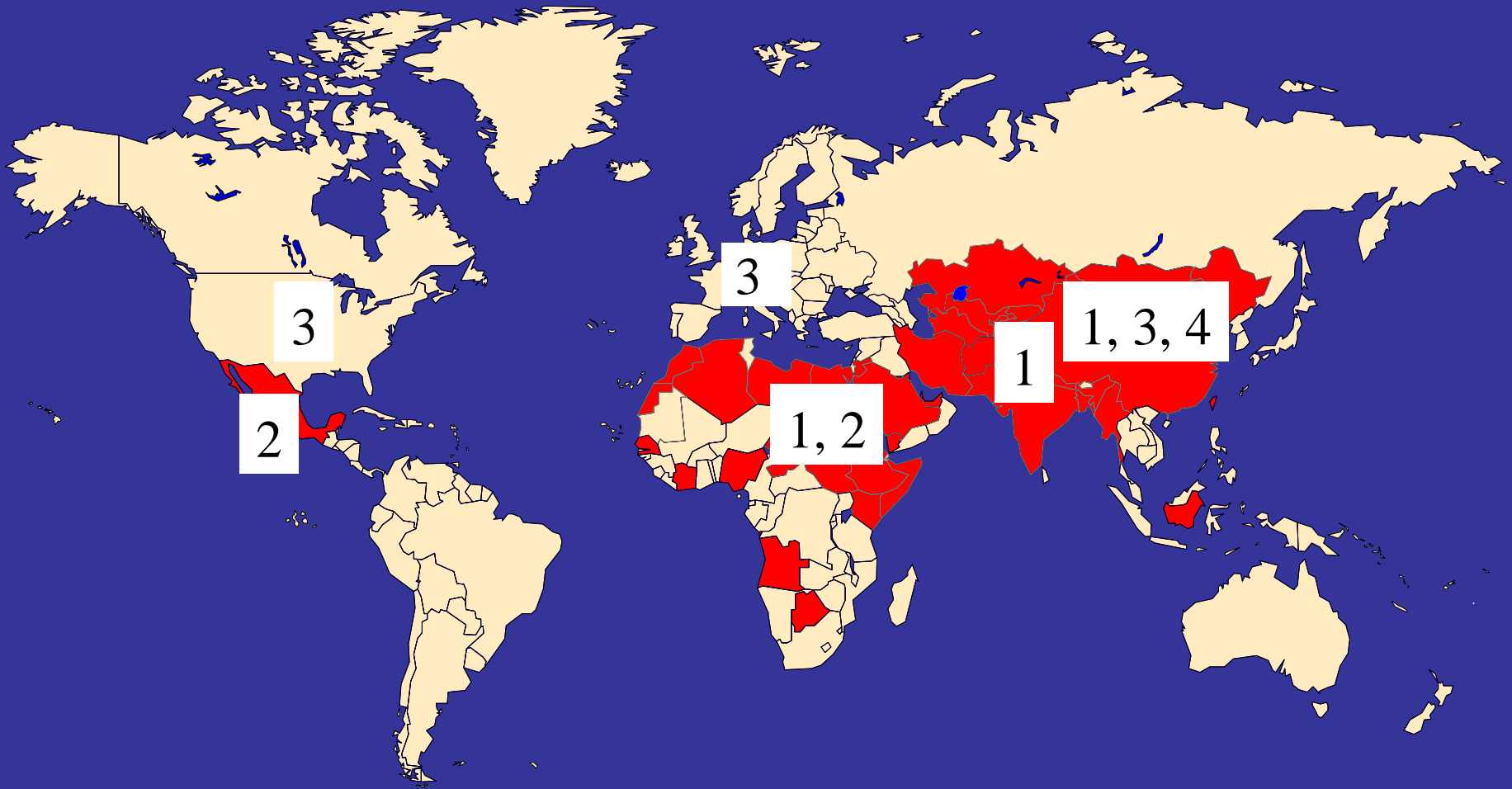


There are four human HEV genotypes

Genotype 1	human cases Asia, Africa
Genotype 2	human cases Mexico, Chad
Genotype 3	human, swine, wild boar, deer and mongooses, world-wide
Genotype 4	human cases, swine and cat Taiwan, Japan, China
Genotype 5	chickens, USA, Brazil, Spain

Geographic Distribution of Hepatitis E

Outbreaks or Confirmed Infection in >25% of Sporadic Non-ABC Hepatitis



HEV genotypes have been subdivided into 24 subgenotypes unfortunately mostly based only on limited sequencing

Genotype 1 a – e

Genotype 2 a – b

complete genome missing for subtype 2b

Genotype 3 a – j

complete genome missing for subtypes 3c – 3f, 3h, 3i

Genotype 4 a – g

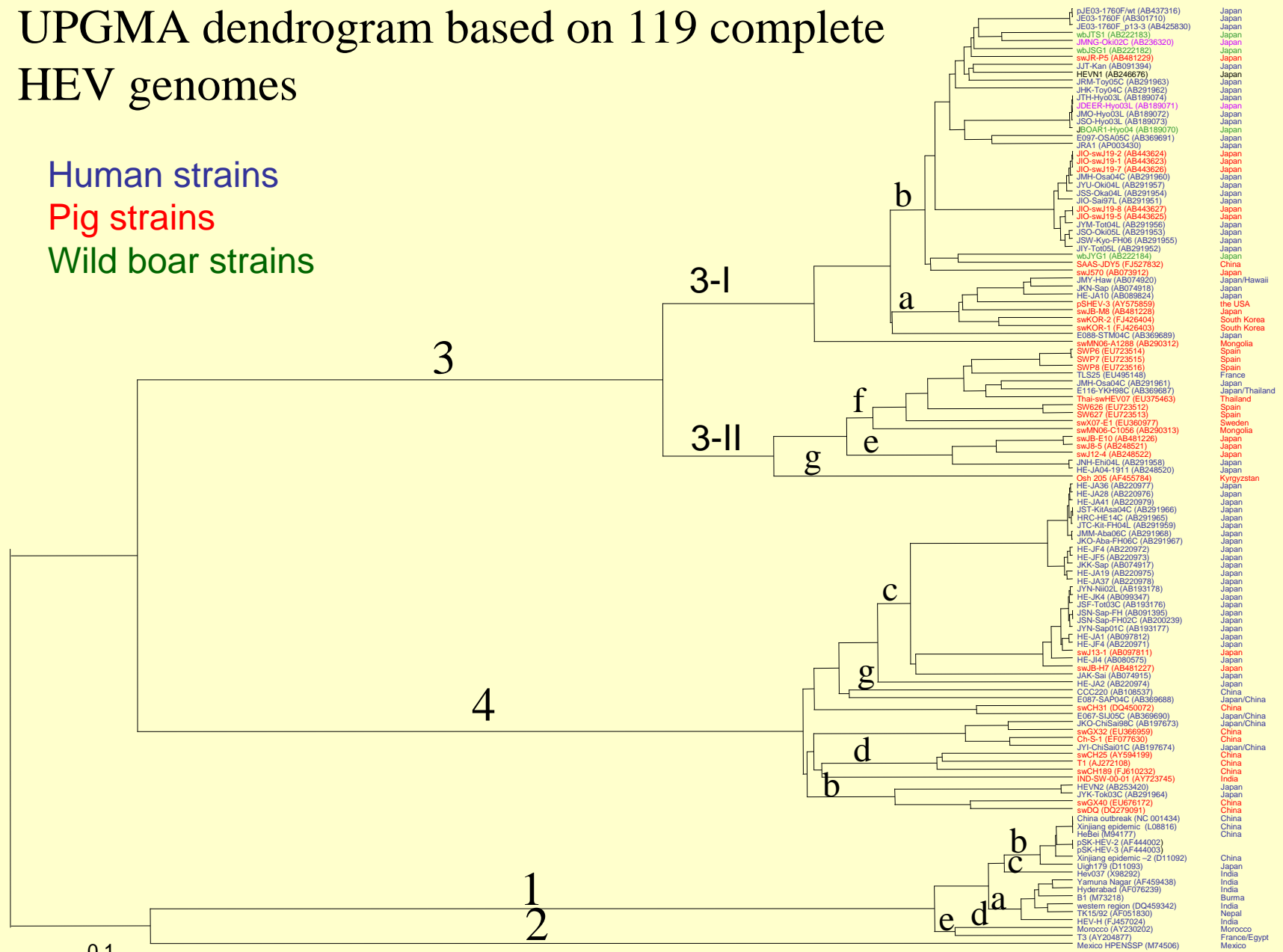
complete genome missing for subtypes 4a, 4b, 4e,

UPGMA dendrogram based on 119 complete HEV genomes

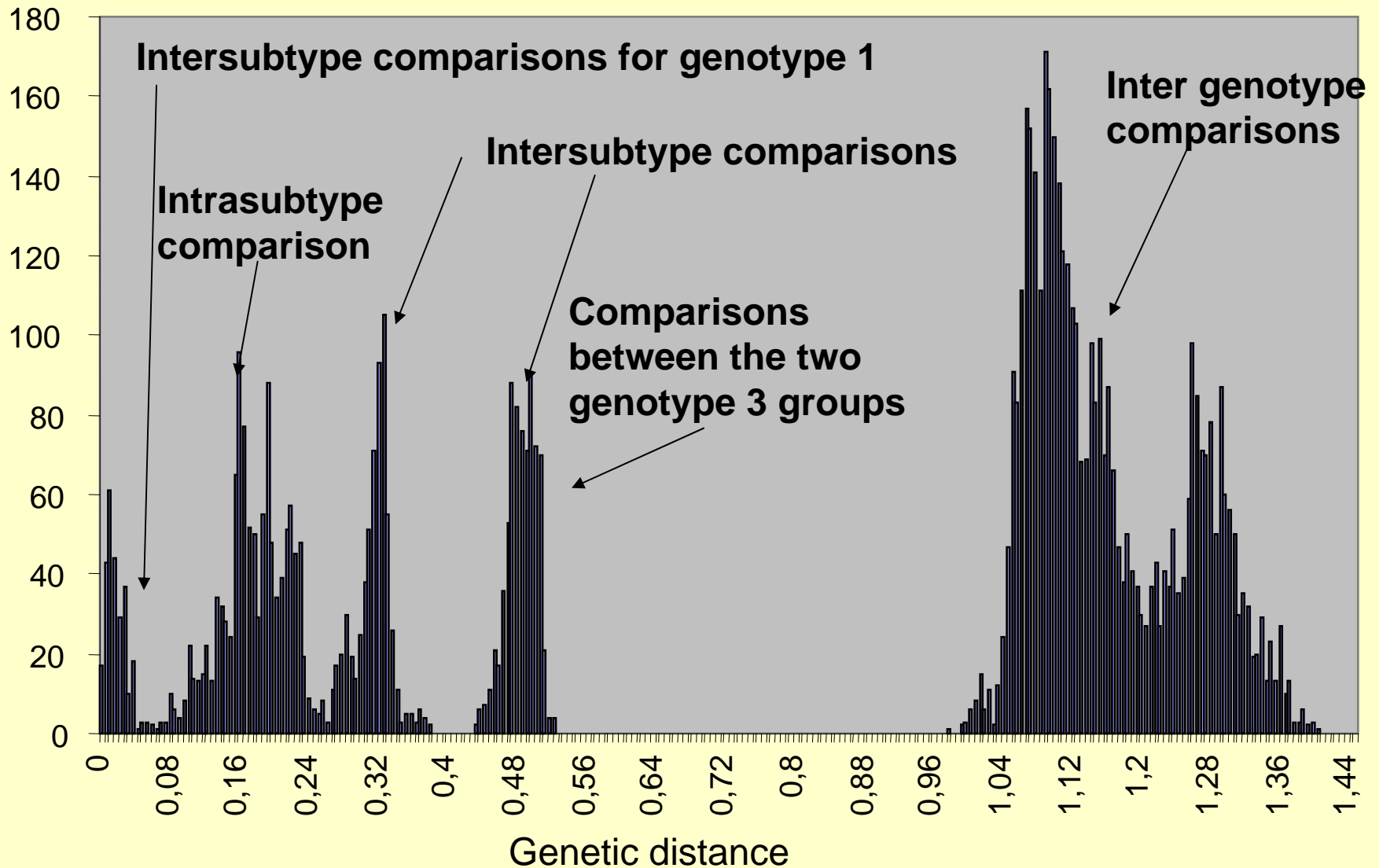
Human strains

Pig strains

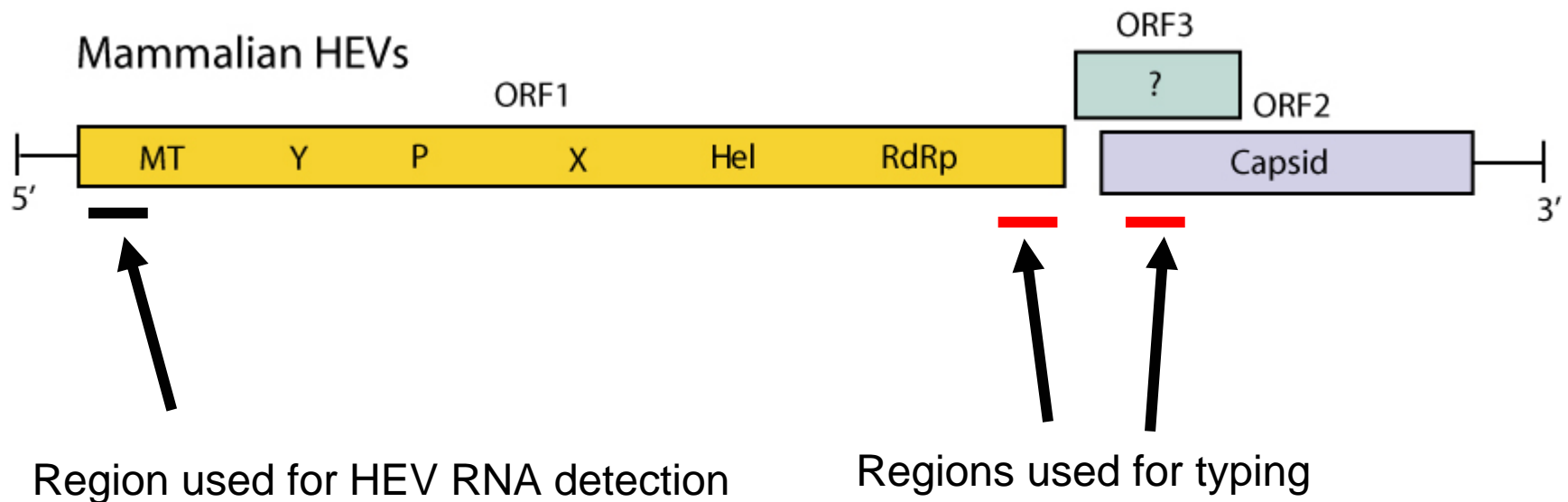
Wild boar strains



Pairwise comparisons of genetic distances between 119 complete HEV genomes

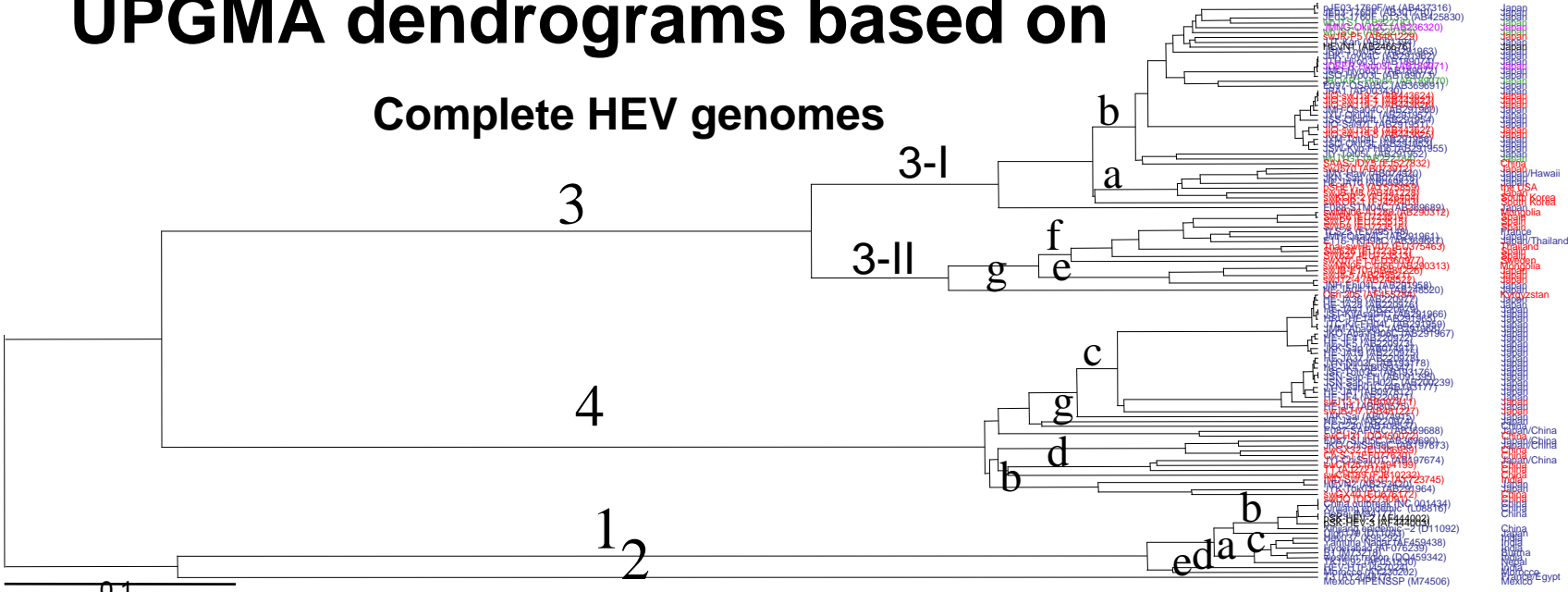


Genomic organization of HEV

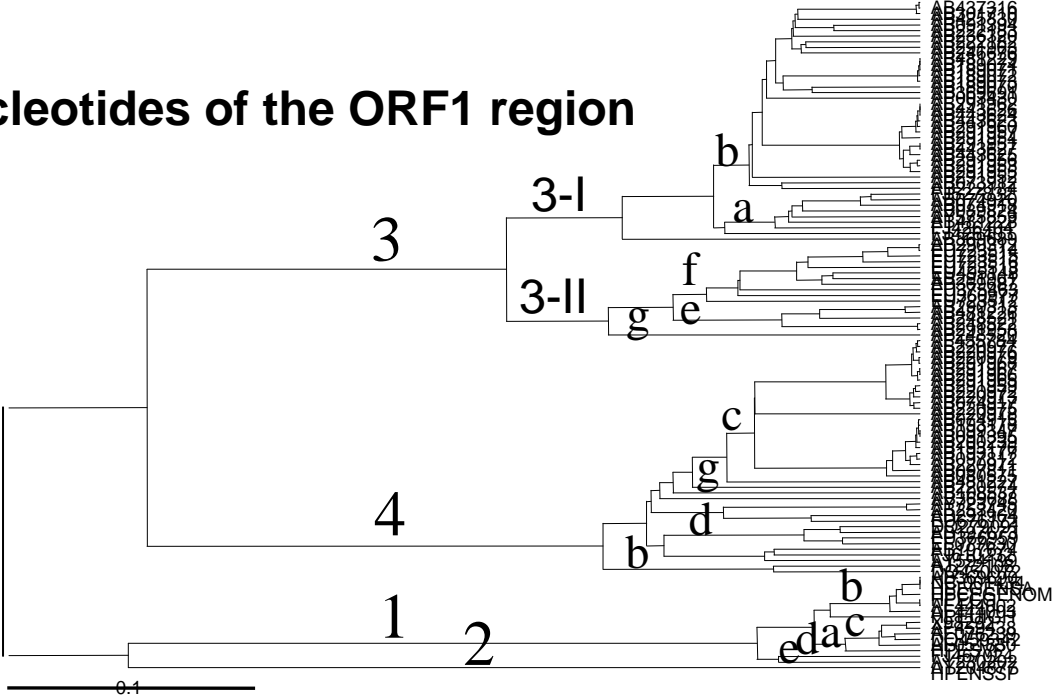


UPGMA dendrograms based on

Complete HEV genomes

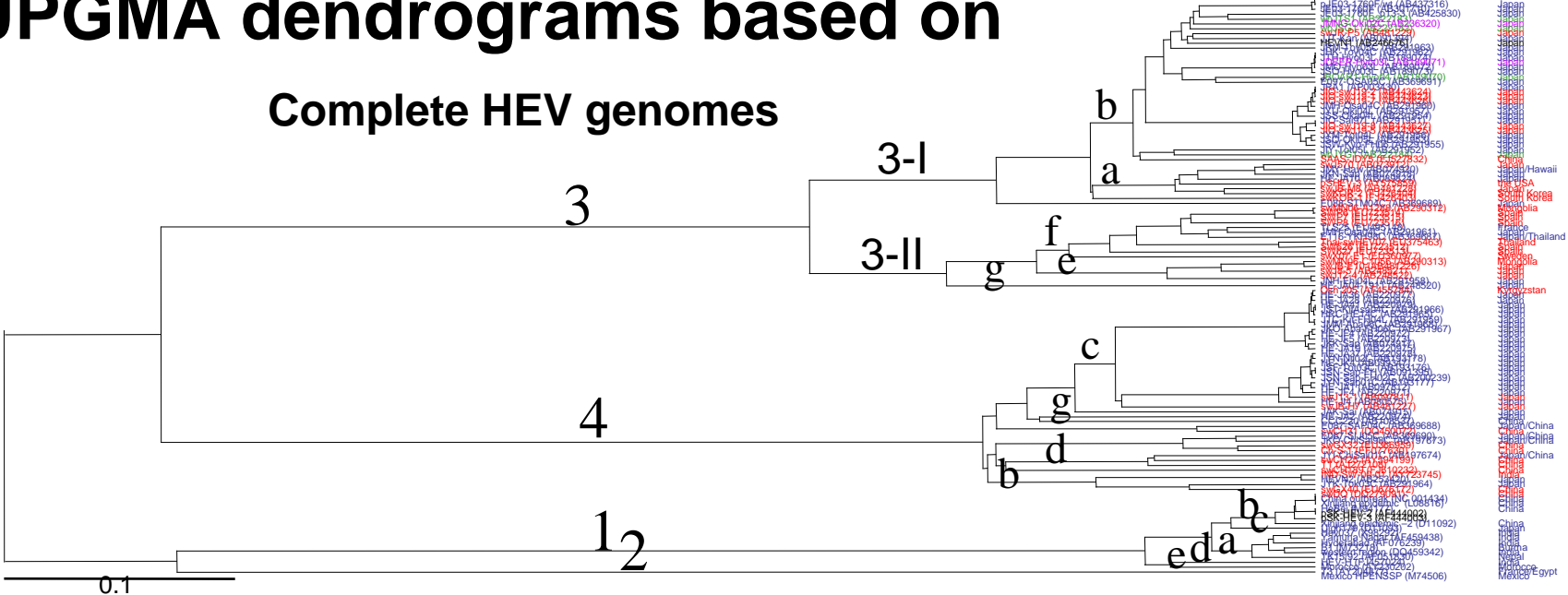


344 nucleotides of the ORF1 region

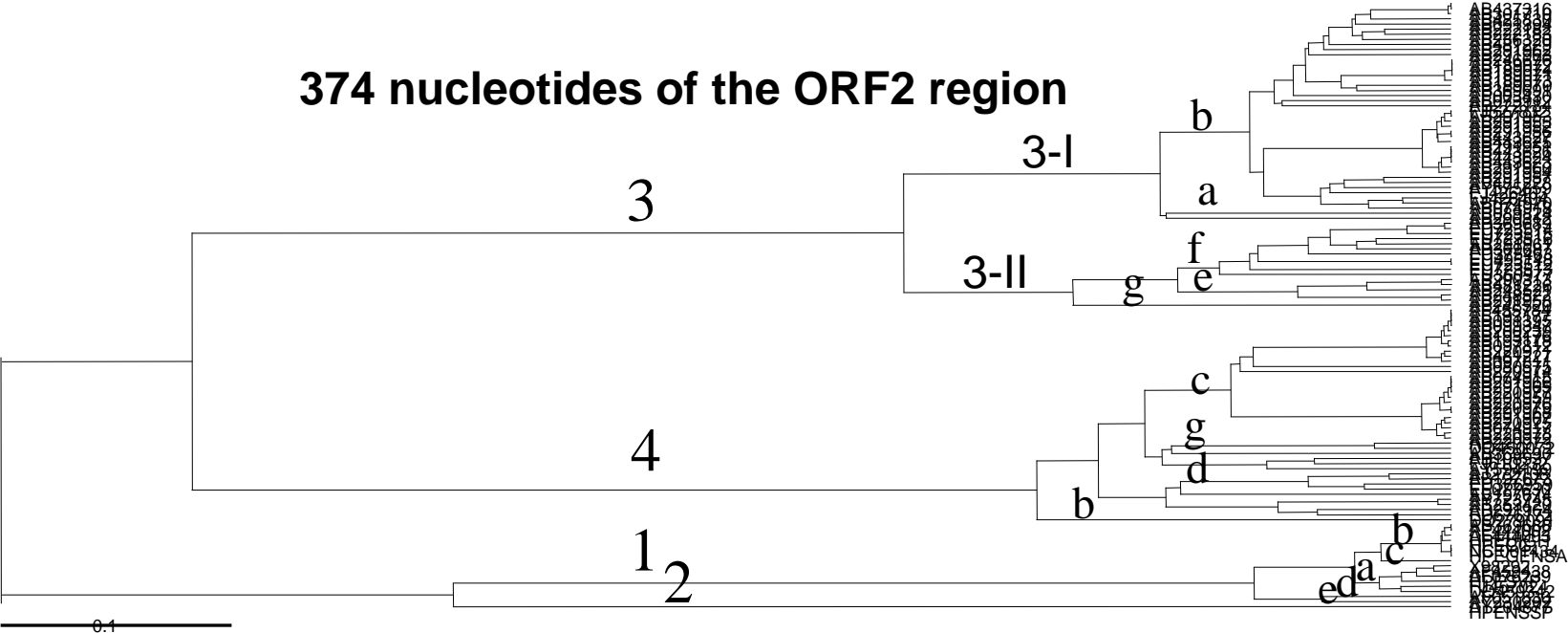


UPGMA dendrograms based on

Complete HEV genomes



374 nucleotides of the ORF2 region



Results from testing sera for HEV RNA from 180 patients with anti- HEV

	HEV IgM positive		only IgG positive	
	N tested	HEV RNA	N	HEV RNA
Sweden	50	43 (86 %)	47	11 (23 %)
Denmark	50	28 (56 %)	33	4 (12 %)
TOTAL	100	71 (71%)	80	15 (19 %)

Hepatitis E virus isolates from 1993- 2008 typed at the Swedish Institute for Infectious Disease Control (SMI)

Geno- type	1993-2003	2004	2005	2006	2007	2008	Total
1	29	6	11	2	6	13	67 (86 %)
3	1	0	1	1	2	6	11 (14 %)
Total	30	6	12	9	17	19	78

Age, sex and country of infection for clinical cases of hepatitis E genotype 3 in Denmark and Sweden

Strain designation	sex	age	country of infection
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Samples from Sweden

26/02	M	60	Sweden
560/05	M	67	Sweden
1459/06	F	62	Spain/Austria
1559/07	F	65	Serbia/Montenegro
668/08	M	49	Sweden

Samples from Denmark

525/07	M	60	Spain
38/08	M	37	Denmark
258/08	M	36	Unknown
392/08	M	44	Denmark
751/08	M	39	Spain
889/08	M	70	Denmark

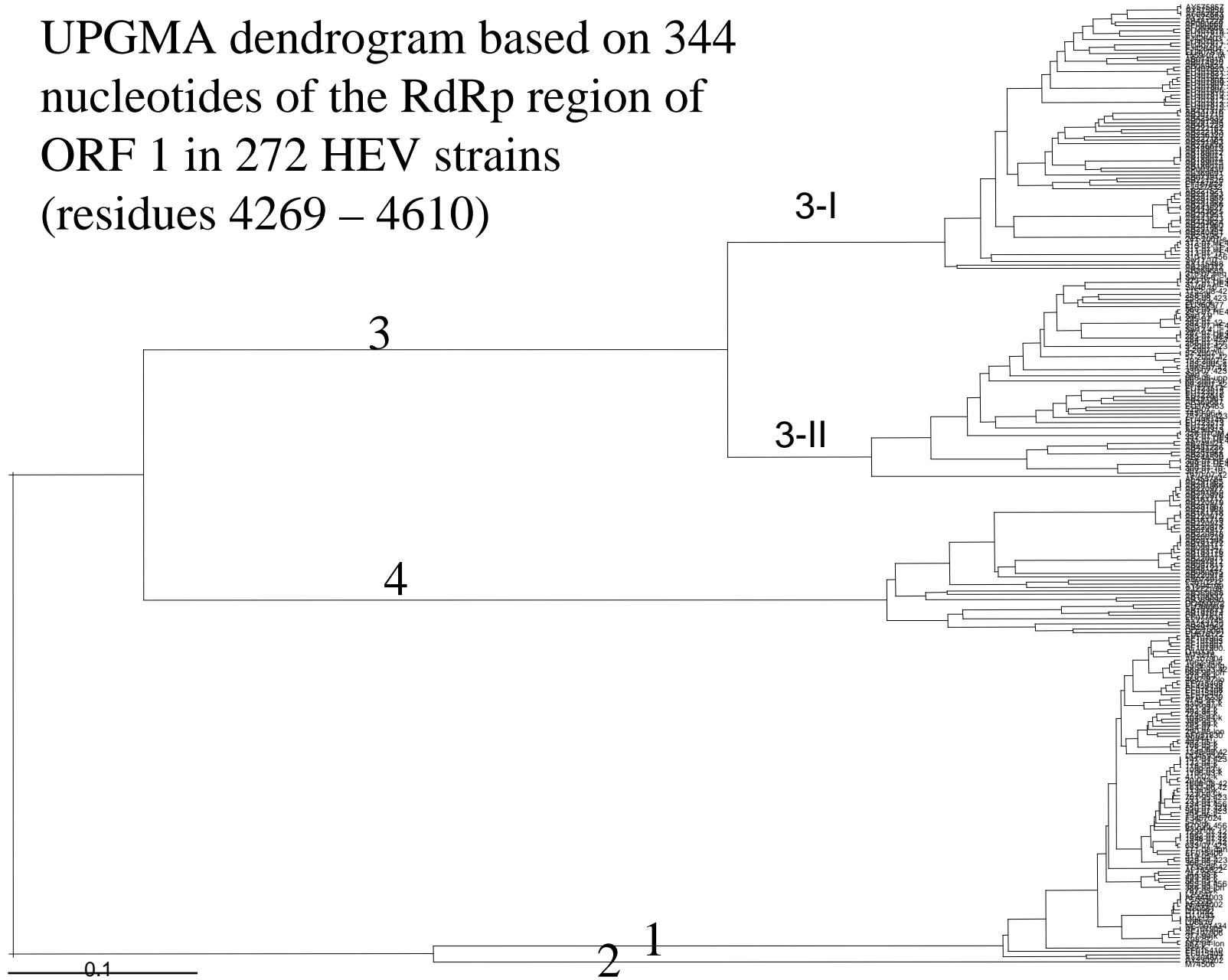
Age and sex of clinical cases of hepatitis E genotype 3 in Europe and the USA

Country	Number (% men)	mean age
England	29 (62 %)	65 (44-82)*
Hungary	27 (55 %)	61 (17 – 78)*
France	21 (67 %)	48 (17- 81)*
Spain	18 (72 %)	57 (39 –80)*
The Netherlands	8 (63 %)	56 (20-84)*
Austria, Germany, Italy, Greece, the USA	5 (80 %)	60 (43 –69)
Sweden	5 (60 %)	61 (49 – 67)
Denmark	6 (100 %)	48 (37 – 70)

*Adapted from Chong Gee Theo 2006

Helène Norder, SMI 2009

UPGMA dendrogram based on 344 nucleotides of the RdRp region of ORF 1 in 272 HEV strains (residues 4269 – 4610)



Conclusions

Complete HEV genomes of the described “new” subtypes are needed

There is a need to re-evaluate some subtypes of HEV

There are two major clades within genotype 3

Group 3-I is mainly formed by strains from Asia and the USA

Group 3-II is mainly formed by strains from Europe

There are geographical clades of HEV strains, with strains intermixed from pigs and humans infected in the same country

The HEV strains from wild boars also cluster according to country

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