



# ICTV Virus Taxonomy Profile: *Hepeviridae* 2022

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## Abstract

The family *Hepeviridae* includes enterically transmitted small quasi-enveloped or non-enveloped positive-sense single-stranded RNA viruses infecting mammals and birds (subfamily *Orthohepevirinae*) or fish (*Parahepevirinae*). Hepatitis E virus (genus *Paslahepevirus*) is responsible for self-limiting acute hepatitis in humans; the infection may become chronic in immunocompromised individuals and extrahepatic manifestations have been described. Avian hepatitis E virus (genus *Avihepevirus*) causes hepatitis-splenomegaly syndrome in chickens. This is a summary of the International Committee on Taxonomy of Viruses (ICTV) Report on the family *Hepeviridae*, which is available at [www.ictv.global/report/hepeviridae](http://www.ictv.global/report/hepeviridae).

**Table 1.** Characteristics of members of the family *Hepeviridae*

Example:	human hepatitis E virus Burma (M73218), species <i>Paslahepevirus balayani</i> , genus <i>Paslahepevirus</i>
Virion	Quasi-enveloped or non-enveloped, 27–34 nm diameter with a single capsid protein
Genome	6.4–7.2 kb capped positive-sense monopartite RNA containing three ORFs
Replication	Occurs in association with the host endoplasmic reticulum
Translation	From genomic (ORF1) and a subgenomic (ORF2 and ORF3) capped mRNA
Host range	Mammals ( <i>Chirohepevirus</i> , <i>Paslahepevirus</i> , <i>Rocahepevirus</i> ), birds ( <i>Avihepevirus</i> ) and salmonid fishes ( <i>Piscihepevirus</i> )
Taxonomy	Realm <i>Riboviria</i> , kingdom <i>Orthornavirae</i> , phylum <i>Kitrinoviricota</i> , class <i>Alsuviricetes</i> , order <i>Hepelivirales</i> : two subfamilies, multiple genera and species

## VIRION

Virions of human hepatitis E virus are icosahedral, quasi-enveloped (blood or tissue culture [1]) or non-enveloped (faeces), spherical particles with a diameter of 27–34 nm (Table 1, Fig. 1a). The capsid is formed by capsomeres consisting of homodimers of a single capsid protein, forming the virus shell. Each capsid protein contains three linear domains forming distinct structural elements: S (the continuous capsid), P1 (three-fold protrusions) and P2 (two-fold spikes). Neutralizing epitopes have been found in the P2 domain. Each domain contains a putative polysaccharide-binding site that may interact with cellular receptors [2].

## GENOME

Viral genomes (Fig. 1b) are positive-sense monopartite RNA of 6.4–7.2 kb, with three ORFs flanked by short 5'- and 3'-terminal non-coding regions: ORF2 (capsid protein) overlaps ORF3 but neither overlaps ORF1. The 5'-end is m<sup>7</sup>G-capped and the 3'-end is polyadenylated (Fig. 2). Non-structural proteins encoded by ORF1 have limited similarity with the 'alpha-like supergroup' of viruses and contain domains consistent with a methyltransferase, papain-like cysteine protease, macro domain, RNA helicase and RNA-directed RNA polymerase [3]. A small immunoreactive protein (12.5 kDa) encoded by ORF3 has been shown to

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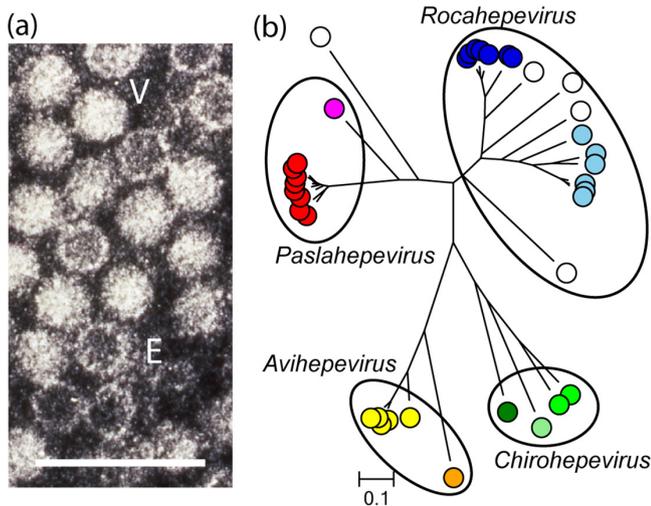
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**Fig. 1.** (a) Negative-contrast electron micrograph of human hepatitis E virus particles from a case stool collected in Nepal. (V) virion and (E) empty capsid. Bar: 100 nm (photograph M. Purdy). (b) Phylogeny of orthohepevirin methyltransferase domains (details: ICTV Report).

exhibit multiple functions associated with virion morphogenesis, egress and viral pathogenesis. The capsid and ORF3 proteins are translated from a subgenomic RNA.

## REPLICATION

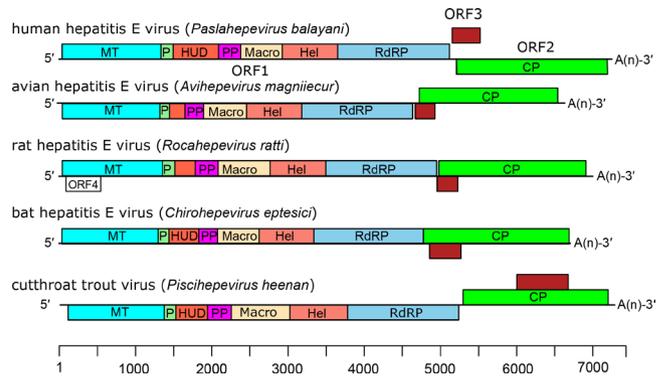
The viral RNA-directed RNA polymerase associates with the host endoplasmic reticulum through residues encoding a predicted transmembrane domain. Replication involves temporal separation and alternating cycles of synthesis of positive- and negative-sense RNAs [3, 4].

## TAXONOMY

Current taxonomy: [ictv.global/taxonomy](http://ictv.global/taxonomy). Members of the subfamily *Orthohepevirinae* infect humans and domestic and wild mammals, (genera *Paslahepevirus* and *Rocahepevirus*), bats (*Chirohepevirus*), and birds (*Avihepevirus*) [5, 6]. Human hepatitis E virus can cause self-limiting acute hepatitis in humans and is transmitted by contaminated water, the consumption of undercooked or raw meat or iatrogenically through blood transfusion or organ transplantation. Globally, human hepatitis E virus is a major cause of acute hepatitis.

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**Fig. 2.** Genome organization of hepeviruses. There are short 5'- and 3'-non-coding regions. The ORF1 polyprotein includes the putative functional domains: MT, methyltransferase; P, a putative papain-like cysteine protease; HUD, hepevirus unique (or Z-) domain; PP, a hypervariable polyproline region; Macro, macro domain; Hel, helicase; and RdRP, RNA-directed RNA polymerase. ORF2 encodes the capsid protein (CP) and ORF3 a small phosphoprotein.

Chronic hepatitis E virus infection has increasingly become an important clinical problem in immunocompromised individuals. Cutthroat trout virus, a member of the subfamily *Parahepevirinae*, infects trout and salmon, although its pathogenicity and full host range are unknown.

## RESOURCES

Full ICTV Report on the family *Hepeviridae* : [www.ictv.global/report/hepeviridae](http://www.ictv.global/report/hepeviridae).

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### Conflicts of interest

The authors declare that there are no conflicts of interest.

### Disclaimer

M. Purdy - CDC/ATSDR has not formally disseminated the conclusions in this report; they do not represent and should not be construed to represent any agency determination or policy.

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