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SECTION B: Viruses

201 Classification of Human Viruses

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The “viral family” concept is fundamentally important in understanding the biologic classification of viruses.¹ By specifying the family to which a virus belongs, a great deal may be inferred about the physical, chemical, and biological properties of that virus as well as its evolutionary relationships and modes of gene expression.² Viral families are designated with the suffix *-viridae*.³ Families are distinguished largely on the basis of physiochemical properties, genome structure, size, morphology, and molecular processes.⁴ Table 201-1 lists some criteria that are used to differentiate human virus families.

Twenty-four virus families have been implicated in human disease;⁵ they are listed in Table 201-2. In some cases, humans serve as a reservoir for the viruses and the link to human disease is clear cut. In other cases, humans may be incidental hosts or the link to disease may be more tenuous. Table 201-3 lists specific viruses within each family that are linked to human disease.

Facilitated by advances in molecular methods, the discovery of new viruses and more careful characterization of known viruses^{6,7} have resulted in frequent changes in family taxonomy. Some examples of such changes include: (1) de novo creation of a virus family (e.g., Anelloviridae);⁸ (2) splitting a new family off of an existing one (e.g., Hepeviridae from Caliciviridae);⁹ (3) dividing a family into two new families (e.g., Papovaviridae into Papillomaviridae and Polyomaviridae);¹⁰ and (4) uniting formerly separate families (e.g., the incorporation of Toroviridae into

Coronaviridae).^{11,12} Working groups¹³ within the International Committee on Taxonomy of Viruses (ICTV)¹⁴ have the responsibility of approving new names and making changes in classification. Figures 201-1, 201-2, and 201-3 illustrate the relationships between human virus families in terms of key biologic criteria listed in Table 201-1.

Families hierarchically are subdivided in a variety of ways including into subfamilies (suffix *-virinae*), genera (suffix *-virus*), and species (suffix *-virus*).¹⁵ In the past, the conventions for naming species were somewhat arbitrary and varied from family to family. The ICTV has instituted a more uniform system. A virus species, as defined by van Regenmortel, is “a polythetic class of viruses that constitutes a replicating lineage and occupies a particular ecologic niche.”¹⁶ *Polythetic* refers to the fact that viruses grouped within a species share many but not all properties in common. Species criteria may include genetic structure, sequence homology, host range, tissue tropism, biological reservoir, route of transmission, immunologic cross-reactivity, epidemiology, and pathogenicity.¹⁷ With the advent of rapid nucleic acid sequencing, sequence homology has taken precedence over other species classification criteria.¹⁸

The current system of species classification does not always correspond to common usage or historical concepts of viral species. For example, the three immunologically distinct viruses targeted by the trivalent poliovirus vaccine are now considered to be the

TABLE 201-1. Major Criteria for Classifying Human Viral Families

Criterion	Basis of Classification
Type of genomic nucleic acid	DNA or RNA
Nucleic acid strandedness	ds, ss, partially ds
"Sense" of ss nucleic acid	+, -, – with ambisense
Capsid morphology	Icosahedral, helical, or complex
Envelope	Present or absent
Genome segmentation	Number of segments
Genomic structure	For example, type of RNA cap, location of structural genes or repeat sequences
Electron micrographic (EM) appearance	For example, bullet-shaped rhabdoviruses or star-shaped astroviruses
Size of virion and/or genome	For example, large genome DNA viruses like pox or herpesviruses versus small genome viruses like picornaviruses, parvoviruses, or hepadnaviruses
Nature of gene expression: (including nature and number of mRNA transcripts)	For example, use of genomic polyproteins (picornaviruses, flaviviruses); use of reverse transcriptase (retroviruses, hepadnaviruses); use of multiple 3' nested genes (coronaviruses); use of RNA ambisense coding (arenaviruses, bunyaviruses)

ds, double stranded; ss, single stranded.

TABLE 201-2. Families of Viruses that Infect Humans²

Name	Derivation of Family Name	Genome	Segmentation	Capsid Morphology	Envelope
Adenoviridae	"Gland"	dsDNA	1	Icosahedral	Naked
Anelloviridae	"Ring-shaped"	ssDNA(-) ^f	1	Icosahedral	Naked
Arenaviridae	"Sand"	ssRNA(-) ^{g,h}	2	Helical	Enveloped
Astroviridae	"Star"	ssRNA(+) ⁱ	1	Icosahedral	Naked
Bornaviridae ^a	Location in Germany	ssRNA(-) ^g	1	Helical	Enveloped
Bunyaviridae	Location in Uganda	ssRNA(-) ^{g,h}	3	Helical	Enveloped
Caliciviridae	"Cup" or "chalice"	ssRNA(+) ⁱ	1	Icosahedral	Naked
Coronaviridae ^b	"Crown"	ssRNA(+) ⁱ	1	Helical	Enveloped
Filoviridae ^a	"Thread"	ssRNA(-) ^g	1	Helical	Enveloped
Flaviviridae	"Yellow"	ssRNA(+) ⁱ	1	Icosahedral	Enveloped
Hepadnaviridae	"Liver", DNA	Partially ssDNA	1	Icosahedral	Enveloped
Hepeviridae	"HEPatitis E"	ssRNA(+) ⁱ	1	Icosahedral	Naked
Herpesviridae ^c	"Creeping"	dsDNA	1	Icosahedral	Enveloped
Orthomyxoviridae	"True"; "slime or mucus"	ssRNA(-) ^g	6–8	Helical	Enveloped
Papillomaviridae	"Bumpy"; "tumor"	dsDNA	1	Icosahedral	Naked
Paramyxoviridae ^a	"Alongside"; "slime or mucus"	ssRNA(-) ^g	1	Helical	Enveloped
Parvoviridae	"Little"	ssDNA	1	Icosahedral	Naked
Picornaviridae ^d	"Little"; RNA	ssRNA(+) ⁱ	1	Icosahedral	Naked
Polyomaviridae	"Many"; "tumor"	dsDNA	1	Icosahedral	Naked
Poxviridae	"Pustule"	dsDNA	1	Complex	Variable
Reoviridae	Respiratory-enteric-orphan	dsRNA	10–12	Icosahedral	Naked
Retroviridae	"Backwards"	ssRNA(+) ⁱ	1 but diploid	Complex	Enveloped
Rhabdoviridae ^a	"Rod"	ssRNA(-) ^g	1	Helical	Enveloped
Togaviridae	"Cloak"	ssRNA(+) ⁱ	1	Icosahedral	Enveloped
(delta) ^e	"Fourth" hepatitis group	ssRNA(-) ^g	1	Icosahedral	Enveloped

^aMononegavirales.^bNidovirales.^cHerpesvirales.^dPicornavirales.^e"Floating genus" – This genus is not currently assigned to a viral family. It bears some similarities to viroid pathogens of plants.^fssDNA(+) indicates the mRNA coding strand.^gssRNA(-) indicates the complement of message sense strand.^hSome segments are ambisense.ⁱssRNA(+) indicates message sense strand.

TABLE 201-3. Human Viral Infections Listed by Family^a

Name	Representative Viruses ^b
Adenoviridae	Human adenovirus types 1 to 57 in seven species (human adenovirus species A to G) ^{22a}
Anelloviridae ^b	TT (transfusion-transmitted or Torque-Teno) virus ^c
Arenaviridae	Lassa virus, lymphocytic choriomeningitis virus, Junin virus, Machupo virus, Guanarito virus, Sabiá virus, Whitewater Arroyo virus, ²³ Chapare virus ²⁴
Astroviridae	Human astroviruses – eight serotypes
Bornaviridae	Borna disease virus (BDV)
Bunyaviridae	California encephalitis virus, Sin Nombre virus, La Crosse virus, Hantaan virus, Muerto Canyon virus, Crimean–Congo hemorrhagic fever virus, Sandfly fever viruses, Rift Valley fever virus, and many others
Caliciviridae	Norwalk and Norwalk-like viruses, Sapporo and Sapporo-like viruses
Coronaviridae	SARS coronavirus, Human coronaviruses OC43, ^{24a} 229E, NL63, ²⁵ and HKU1; ²⁶ human torovirus and other human enteric coronaviruses
Filoviridae	Ebola viruses (e.g. Ebola Zaire), Marburg virus
Flaviviridae	Genus Alphavirus: dengue virus, yellow fever virus, Japanese encephalitis virus, West Nile virus, Murray Valley encephalitis virus, Kyasanur encephalitis virus, tick-borne encephalitis virus, Zika virus, and others Genus Hepacivirus: hepatitis C virus (HCV) Genus Pegivirus: ^d GB virus-C ^e (GBV-C, formerly hepatitis G virus or HGV) ^{26a}
Hepadnaviridae	Hepatitis B virus (HBV)
Hepeviridae ^g	Hepatitis E virus (HEV)
Herpesviridae	Herpes simplex virus type 1, herpes simplex virus type 2, varicella-zoster virus, cytomegalovirus, Epstein–Barr virus, human herpesvirus 6, human herpesvirus 7, human herpesvirus 8 (Kaposi sarcoma-associated herpesvirus), herpes simian B virus
Orthomyxoviridae	Influenza A virus (e.g. subtype H1N1), influenza B virus, influenza C virus, Thogoto virus, Dhori virus ^{26b}
Papillomaviridae	Human papilloma virus – more than 150 types of varying oncogenicity ^{26c}
Paramyxoviridae	Measles (rubeola) virus, mumps virus, respiratory syncytial virus, parainfluenza viruses, human metapneumoviruses, Hendra virus, Nipah virus, Menangle virus ²⁷
Parvoviridae	Human parvovirus B-19, human bocavirus, ²⁸ adeno-associated viruses ^{c,g}
Picomaviridae ^{28a}	Genus Enterovirus: human rhinoviruses (more than 100 serotypes), enteroviruses (including poliovirus 1–3, coxsackie A and B viruses, echoviruses, other human enteroviruses) Genus Hepatovirus: hepatitis A virus (HAV) Genus Parechovirus: human parechoviruses Genus Kobuvirus: Aichi virus Genus Cosavirus: human cosaviruses ²⁹ Genus Cardiovirus: Vilyuisk humanencephalomyelitis virus, Saffold viruses ³⁰ Genus Salivirus: human klassevirus, ³¹ salivirus A Genus Senecavirus: Seneca Valley virus ^f Unassigned: Syr-Darya Valley fever virus
Polyomaviridae	JC virus, BK virus, KI virus, WU virus, Merkel cell polyomavirus, lymphotropic polyomavirus, human polyomavirus 6, human polyomavirus 7, trichodysplasia spinulosa-associated polyomavirus, human polyomavirus 9 ^{32,32a}
Poxviridae	Molluscum contagiosum virus, variola (smallpox) virus, monkeypox virus, vaccinia virus, orf virus, pseudocowpox virus, Tanapox virus, Yaba monkey tumor virus ^{32b}
Reoviridae	Human rotavirus, Colorado tick fever virus, human reovirus, ^c Kemerovo virus
Retroviridae	Human immunodeficiency viruses 1 and 2, human T-lymphocyte lymphotropic viruses, ³³ xenotropic murine leukemia virus-related virus, ^g human endogenous retroviruses (HERVs), simian foamy virus
Rhabdoviridae	Rabies virus, vesicular stomatitis virus
Togaviridae	Rubella virus; eastern equine, western equine, and Venezuelan equine encephalitis viruses; Ross River, Sindbis, and Semliki Forest viruses
(Delta) ^h	Hepatitis delta virus ^e (HDV)

^aExamples listed correspond to common usage and do not necessarily comply with the official ICTV designations of virus species.

^bSome zoonoses are included.

^cOrphan virus for which a link to human disease has not been determined.

^dProposed genus name.

^eSatellite virus requiring coinfection with heterologous virus for replication.

^fPorcine virus being used clinically in humans as an oncolytic agent.³⁴

^gPossible laboratory contaminant.

^h"Floating genus", See Table 201-2.

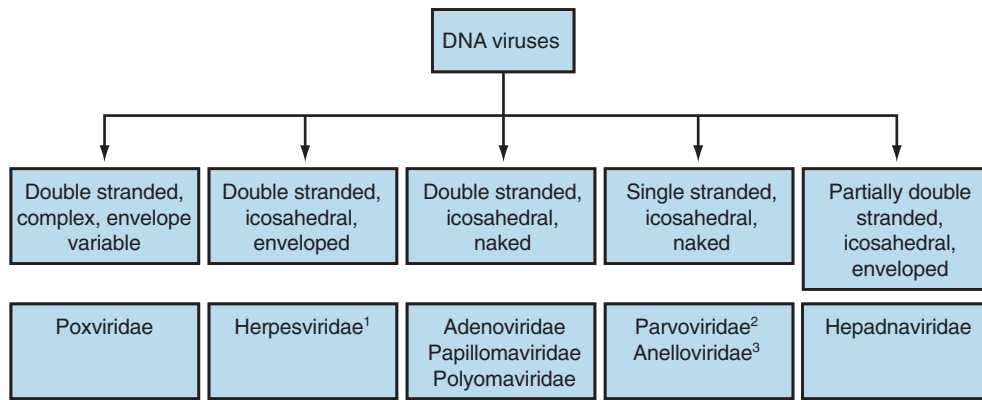


Figure 201-1. Organizational chart of the eight human virus families with DNA genomes. The chart groups virus families using the strandedness of the viral genome, the structure of the capsid, and the presence or absence of an envelope. All of these viruses are nonsegmented. Like retroviruses, hepadnaviruses contain reverse transcriptase.

¹This family of viruses has been assigned to the Herpesvirales order of viruses.

²Parvoviruses vary in the percentage of positive and negative sense ssDNA genomes that are packaged, depending on the genus.

³Anelloviruses package negative sense ssDNA genomes. This is the strand that will be transcribed into mRNA.

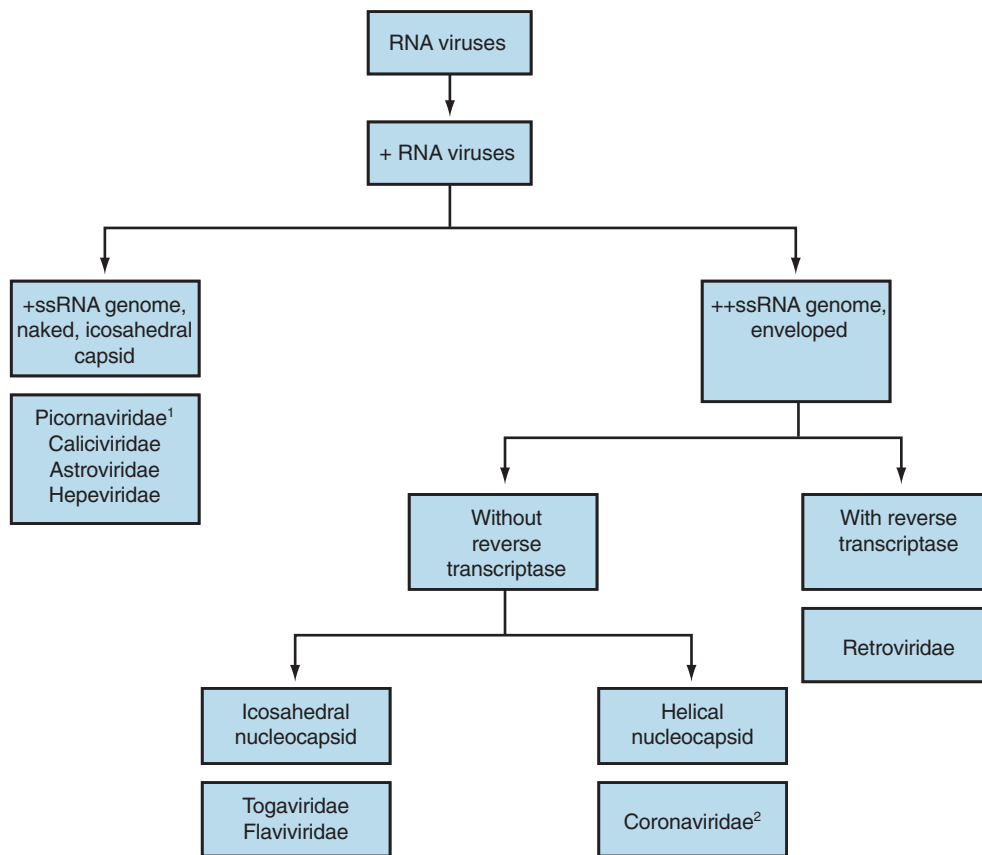


Figure 201-2. Organizational chart of the eight human virus families with positive-sense RNA (mRNA-like) genomes. The chart groups virus families using the presence or absence of an envelope, the presence of reverse transcriptase, and the structure of the capsid. All of these viruses have a single-stranded, nonsegmented viral genome.

¹This family of viruses has been assigned to the Picornavirales order of viruses.

²This family of viruses has been assigned to the Nidovirales order of viruses.

same species: human enterovirus C.^{19,20} This species includes at least 18 additional serotypes with diverse clinical presentations.^{20a} The practicality of distinguishing such serotypes is emphasized by the eradication of wild poliovirus type 2 in 2000.²¹

Species can be subdivided further into groups, clades, types, subtypes, serotypes, variants, and isolates – depending on the family involved and the degree of similarity. Selected

representatives called “type viruses” may be used to illustrate the properties of a particular taxon.

A number of virus families now are assigned to higher level “orders” designated with the suffix *-virales*. Examples are Herpesvirales, Mononegavirales, Picornavirales, and Nidovirales.²² These are indicated by footnotes in Table 201-2. Most families currently are unassigned to orders.

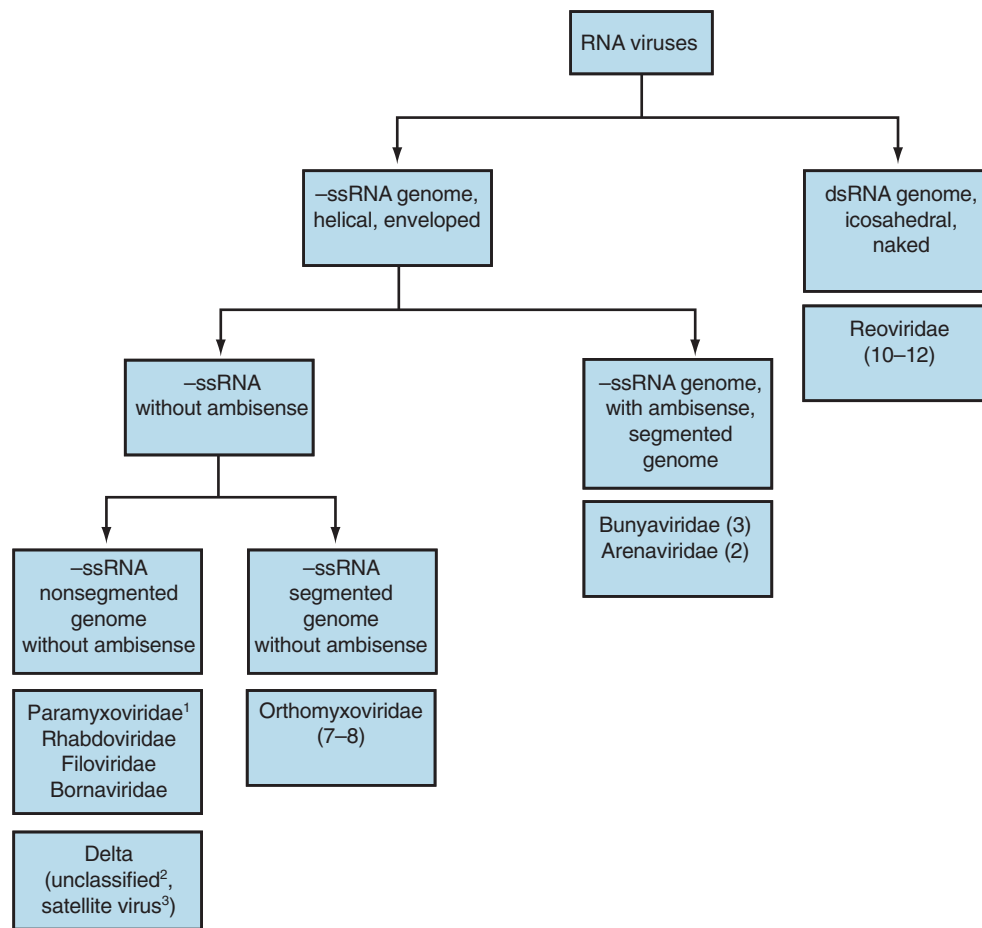


Figure 201-3. Organizational chart of the remaining eight human RNA virus families including the negative singled-stranded (complementary to message sense) and double-stranded RNA viruses. The chart groups the families using the structure of the genome, presence or absence of an envelope, and the presence or absence of ambisense gene expression. For segmented viruses, the number of genome segments is listed in parentheses.

¹This group of virus families is assigned to the Mononegavirales (for monosegmented, negative stranded, order of viruses) order of viruses.

²"Floating genus" – This genus is not currently assigned to a viral family. It bears some similarities to viroid pathogens of plants.

³Satellite virus refers to the fact that hepatitis D virus (HDV) is dependent upon HBV, a genomically unrelated virus for its successful replication.

BOX 201-1. Common Routes of Viral Transmission to Humans

- Respiratory (droplet, aerosol, respiratory secretions on the hands and elsewhere, oral exchange): e.g., influenza virus, varicella-zoster virus, human rhinovirus, human adenovirus, respiratory syncytial virus, parainfluenza virus, metapneumovirus
- Fecal-oral: e.g., polioviruses, Coxsackie viruses, hepatitis A virus, rotavirus, astrovirus, Norwalk virus
- Direct contact: e.g., human papillomavirus (HPV), molluscum contagiosum, HSV-1
- Sexual: e.g., HIV-1, HTLV-1, HBV, HPV 16 & 18, HSV-2
- Urine-associated: e.g., CMV
- Parenteral (blood and blood products, transplantation, tattooing, and scarification): e.g., HIV-1, HBV, HCV
- Animal bite: e.g., rabies virus
- Vertical (germline, intrauterine, perinatal, human milk): e.g. HIV-1, HTLV-1, germline transmission of endogenous retroviruses
- Arthropod-borne (mosquitos, ticks, sandflies): e.g., Japanese encephalitis virus, West Nile virus, dengue virus, yellow fever virus, and many others
- Rodent-associated: e.g., lassa fever virus, sin nombre and other hanta viruses
- Bat-associated transmission: e.g., rabies virus, Nipah virus, Ebola virus, SARS CoV
- Monkey associated: e.g., herpes B virus, monkeypox virus, orf virus
- Other zoonotic associations (cows, sheep, etc.): e.g., orf virus, cowpox virus

In addition to biologic classification, viruses often are categorized according to their clinical presentation (syndromic classification), epidemiology, or mode of transmission. **Box 201-1** lists the major routes of transmission in humans, with representative examples of viruses transmitted by each route.

Understanding viral classification can lead to important generalizations regarding the prevention and treatment of viral

infection as well as insights into the distribution and evolution of viruses.

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