

The family *Herpesviridae*: an update

Experiencing the universe is not the same
as systematizing it, no more than experiencing
love is the same as analyzing it.

Andre Malraux, *La Tentation de l'occident*

Introduction

More than 10 years have elapsed since the first report of the International Committee for the Taxonomy of Viruses (ICTV) Herpesvirus Study Group [187]. In that publication the Study Group designated *Herpesviridae* as the name of the herpesvirus family, erected three subfamilies, the *Alphaherpesvirinae*, *Betaherpesvirinae*, and *Gammaherpesvirinae*, and provided guidelines for the classification of herpesviruses into these subfamilies. Since that publication, the ICTV has approved the recommendation of previous Herpesvirus Study Groups to erect several genera. More important from the point of view of taxonomy and classification of herpesviruses, considerable amounts of new information regarding herpesviruses have accumulated in the past 10 years. Thus, (a) a large number of new herpesviruses has been discovered, (b) a few herpesviruses turned out to be contaminants, most likely derived from calf serum containing a bovine herpesvirus, (c) several herpesvirus genomes have been sequenced, (d) many highly conserved genes have been identified both within the family and in the individual subfamilies, and (e) we have a much better understanding at least of the problems facing the task of classifying herpesviruses. This paper updates the 1981 report.

Definition

Properties of herpesviruses: definition of the family Herpesviridae

Architecture of the virion

Inclusion of viruses into the family *Herpesviridae* is based on the architecture of the virion. A typical herpesvirion consists of (a) a core containing a linear double stranded DNA which, in some instances, forms a torus [84, 163], (b) an icosadeltahedral capsid approximately 100 to 110 nm in diameter containing 12 pentameric and 150 hexameric capsomeres, the latter with a hole running down the long axis [81, 231, 147]; (c) an amorphous, sometimes asymmetric material which surrounds the capsid and which was designated as the tegument [188]; and (d) a membrane designated as the envelope, in which viral glycoprotein spikes are embedded and project from its surface [4, 12, 75, 78, 99, 159, 160, 208, 209, 211].

The reported size of herpesvirions estimated from negatively stained preparations ranges from 120 to nearly 300 nm [188]. One possible explanation for this variability is the thickness of the tegument. The major source of variability, however, is the integrity of the envelope. Virions with intact envelopes are impermeable to negative stain and generally retain a

Table 1. Viruses comprising the family *Herpesviridae*

Designation	Common name (synonyms)	Sub- family	Genome		References
			G + C (mole %)	Group ^a Size (kbp)	
Viruses of humans					
Human herpesvirus 1	herpes simplex virus 1	α	68.3	E	96, 148, 189, 199
Human herpesvirus 2	herpes simplex virus 2	α	69	E	189, 199
Human herpesvirus 3	varicella-zoster virus	α	46	D	57, 68, 189, 226
Human herpesvirus 4	Epstein-Barr virus	γ	60	C	6, 76, 120
Human herpesvirus 5	cytomegalovirus	β	57	E	45, 206, 207, 213
Human herpesvirus 6		β	42	A	132-134, 142, 196
Human herpesvirus 7		β			88
Viruses of nonhuman primates^b					
Aotine herpesvirus 1	HV aotus type 1	β	55	E	1, 54, 69
Aotine herpesvirus 3	HV aotus type 3	β	56	D	69
Cercopithecine herpesvirus 1	B virus, HV simiae	α	75	E	192, 193
Cercopithecine herpesvirus 2	SA8	α	67	E	94
Cercopithecine herpesvirus 3	SA6	β	51		94, 140
Cercopithecine herpesvirus 4	SA15	β			140
Cercopithecine herpesvirus 5	African green monkey cytomegalovirus	β			17
Cercopithecine herpesvirus 6	Liverpool vervet monkey virus	α	52		49
Cercopithecine herpesvirus 7	patas monkey HV; MMV or PHV delta HV	α			146
Cercopithecine herpesvirus 8	rhesus monkey cytomegalovirus	β	52		5
Cercopithecine herpesvirus 9	Medical Lake macaque HV; simian varicella HV	α			18
Cercopithecine herpesvirus 10	rhesus leukocyte assoc. HV strain I				85
Cercopithecine herpesvirus 12	HV papio, baboon HV	γ	-	C	77, 103

Cercopithecine herpesvirus 13	herpesvirus cyclopiis				110
Cercopithecine herpesvirus 14	African green monkey EBV-like virus				18
Cercopithecine herpesvirus 15	rhesus EBV-like HV				181
Ateline herpesvirus 1	spider monkey HV	72			94, 108
Ateline herpesvirus 2	HV ateles	48	B		59, 79, 80, 154
Callitrichine herpesvirus 1	HV saguinus				153
Callitrichine herpesvirus 2	SSG, marmoset cytomegalovirus				168
Cebine herpesvirus 1	capuchin HV (AL-5)				131
Cebine herpesvirus 2	capuchin HV (AP-18)				193
Pongine herpesvirus 1	chimp. HV; pan HV	—	C		102, 127
Pongine herpesvirus 2	orangutan HV				182
Pongine herpesvirus 3	gorilla HV				166
Saimirine herpesvirus 1	marmoset HV; HV M, herpes T, HV tamarinus, HV platyrrhinae type	67	D		94, 105, 130
Saimirine herpesvirus 2	squirrel monkey HV, HV saimiri	46	B		22, 51, 223
Viruses of other mammals					
<i>Bovidae</i>					
Bovine herpesvirus 1	infectious bovine rhinotracheitis HV	72	D		3, 90, 139, 145
Bovine herpesvirus 2	bovine mammillitis virus; Allerton virus, pseudo-lumpy skin disease HV	64	E		36, 37, 143, 214
Bovine herpesvirus 4	Movar HV	50	B		9, 33, 220, 222
Bovine herpesvirus 5	bovine encephalitis HV	72	D		24, 73, 86
Ovine herpesvirus 1	sheep pulmonary adenomatosis associated HV		D		61, 62, 138
Ovine herpesvirus 2	sheep assoc. malignant catarrhal fever of cattle HV		B		28
Caprine herpesvirus 1	goat HV				74, 195
Alcelaphine herpesvirus 1	wildebeest HV, malignant catarrhal fever HV of European cattle	61	B		26, 27, 173, 174

Table 1 (continued)

Designation	Common name (synonyms)	Sub- family	Genome		References
			G + C (mole %)	Group ^a Size (kbp)	
Alcelaphine herpesvirus 2	hartbeest HV	γ	—	B	185
Cervid herpesvirus 1	red deer HV	α	—	D	109, 165
Cervid herpesvirus 2	reindeer (<i>Rangifer taramodus</i>) HV	α	—	D	72
<i>Canidae</i>					
Canid herpesvirus 1	canine HV	α	32		215
<i>Caviidae</i>					
Caviid herpesvirus 1	guinea pig HV 1, Hsiung-Kaplow virus, GPHLV	γ	60		15, 81, 107, 162
Caviid herpesvirus 2	guinea pig cytomegalovirus	β	57		100, 156
Caviid herpesvirus 3	guinea pig HV 3, GPXV				16
<i>Cricetidae</i>					
Cricetid herpesvirus	hamster HV	β			Smith, 59
<i>Elephantidae</i>					
Elephantid herpesvirus	elephant (loxodontal) HV				10, 175
<i>Equidae</i>					
Equid herpesvirus 1	equine HV 1; equine abortion HV	α	57	D	2, 180, 227
Equid herpesvirus 2	equine HV 2; equine cytomegalovirus	β	57	A	31, 32, 176
Equid herpesvirus 3	equine HV 3; equine coital exanthema virus	α	66	D	136, 216, 219
Equid herpesvirus 4	equine HV 4; equine rhinopneumonitis virus	α	56	D	53, 194, 217
Equid herpesvirus 5	equine HV 5	β			30
Equid herpesvirus 6	asinine HV 1	α			111
Equid herpesvirus 7	asinine HV 2	β			29
Equid herpesvirus 8	asinine HV 3	α			29

Table 1 (continued)

Designation	Common name (synonyms)	Sub- family	Genome		References
			G + C (mole %)	Group ^a Size (kbp)	
<i>Suidae</i>					
Suid herpesvirus 1	pseudorabies virus, Aujeszky's disease	α	74	D	13, 97, 172
Suid herpesvirus 2	inclusion-body rhinitis virus, pig cytomegalovirus	β			128, 224
<i>Tupaïidae</i>					
Tupaïid herpesvirus 1	tree shrew HV		66	F	55, 125, 147, 157
Viruses of birds					
<i>Anatidae</i>					
Anatid herpesvirus 1	duck plague HV	α			11, 25
<i>Accipitridae</i>					
Accipitrid herpesvirus 1	bald eagle HV				66
<i>Ciconiidae</i>					
Ciconiid herpesvirus 1	black stork HV				117
<i>Columbidae</i>					
Columbid herpesvirus 1	pigeon HV-1		59		50, 129
<i>Falconidae</i>					
Falconid herpesvirus 1	falcon inclusion body disease virus				141
<i>Gallidae</i>					
Gallid herpesvirus 1	infectious laryngo- tracheitis virus	α	46	D	52, 129, 175, 144
Gallid herpesvirus 2	Marek's disease HV 1		47	E	44, 47, 83, 218
Gallid herpesvirus 3	Marek's disease HV 2				39, 202
<i>Gruidae</i>					
Gruid herpesvirus 1	crane HV				41
<i>Meleagridae</i>					
Meleagrid herpesvirus 1	turkey HV 1	γ	48	E	118, 129

<i>Perdiciid</i>					
Perdiciid herpesvirus 1		bobwhite quail HV		116	
<i>Phalacrocoracidae</i>					
Phalacrocoracid herpesvirus 1	58	cormorant HV; Lake Victoria, cormorant HV		87, 129	
<i>Psittacidae</i>					
Psittacid herpesvirus 1		parrott HV; recently rediscovered Pacheco's disease virus		203	
<i>Sphenicidae</i>					
Sphenicid herpesvirus 1		black footed penguin HV		122	
<i>Strigidae</i>					
Strigid herpesvirus 1	61	owl hepatosplenitis virus		40, 129, 198	
Viruses of amphibia and reptiles					
<i>Boidae</i>					
Boid herpesvirus 1 ^d		boa herpesvirus		101	
<i>Cheloniidae</i>					
Chelonid herpesvirus 1 ^d of green sea turtle		gray patch disease agent		98, 184	
Chelonid herpesvirus 2 ^d		Pacific pond turtle HV		82	
Chelonid herpesvirus 3 ^d		painted turtle HV, map turtle HV		51, 113	
Chelonid herpesvirus 4 ^d		<i>Geochelone chilensis</i> HV, <i>Geochelone carbonaria</i> HV, Argentine turtle HV		112	
<i>Elapidae</i>					
Elapid herpesvirus		Indian cobra HV, banded krait, siamese cobra HV		137, 158	
<i>Iguanidae</i>					
Iguanid herpesvirus 1		green iguana HV		48, 235	
<i>Lacertidae</i>					
Lacertid herpesvirus 1		green lizard HV		183	
<i>Ranidae</i>					
Ranid herpesvirus 1	46	Lucké frog HV		95, 135, 225	
Ranid herpesvirus 2	56	frog HV 4		95, 178	

Table 1 (continued)

Designation	Common name (synonyms)	Sub- family	Genome		References
			G + C (mole %)	Group ^a Size (kbp)	
Viruses of bony fishes					
<i>Cyprinidae</i>					
Cyprinid herpesvirus	carp pox HV				201
<i>Esocidae</i>					
Esocid herpesvirus ^d	northern pike HV				234
<i>Ictaluridae</i>					
Ictalurid herpesvirus 1	Channel catfish HV	α	56	A	43, 46, 232
<i>Percidae</i>					
Percid herpesvirus 1	walleye epidermal hyperplasia virus				119
<i>Pleuronectidae</i>					
Pleuronectid herpesvirus	HV scophthalmus, turbot HV				35
<i>Salmonidae</i>					
Salmonid herpesvirus 1	HV salmonis				233
Salmonid herpesvirus 2	<i>Oncorhynchus masou</i> HV				121

^a A-F Genome arrangements described in the text

^b Aotine herpesvirus 2 [34, 67] and feline herpesvirus 2 [221] have been identified as BHV4. In accordance with the rules this number cannot be assigned to another herpesvirus

^c Bovine herpesvirus 3 sometimes referred to as bovine herpesvirus 4 does not exist. These designations were applied to the virus acquired by cattle from the wildebeest in which it causes malignant catarrhal fever. The wildebeest virus is now called alcelaphine herpesvirus 1

^d Indicates reports of herpesvirus-like particles in tissues but virus was not isolated in cell culture

^e The inclusion of this virus in the list is provisional and subject to verification of lack of identity with other murine herpesviruses

quasi-spherical shape. Virions with damaged envelopes are permeable to negative stain and have a sunny-side-up egg appearance with an irregular shape and a diameter generally larger than that of an intact virion.

Herpesvirus genomes

The majority of herpesvirus DNAs extracted from virions are largely linear, double stranded molecules and those that have been studied in detail appear to have a 3' single nucleotide extension [186, 189]. In the case of human herpesvirus 1 (HHV1, herpes simplex virus 1), and we assume this to be a general case, the DNA circularizes immediately upon release from capsids into the nuclei of infected cells [177]. The DNAs differ with respect to their size and base composition. The size of herpesvirus DNAs varies from approximately 124 to 235 kbp (Table 1). The size of the viral genomes is characteristic of each virus (species) and is not a reflection of polymorphism even though individual herpesvirus genomes vary slightly in size. The differences in the size of the genomes of independent isolates of the same virus species may be as high as 10 kbp and most frequently reflect the number of terminal and/or internal reiterated sequences. Spontaneous deletions also occur; they have been noted in both HHV1 and human herpesvirus 4 (HHV4, Epstein Barr virus or EBV) strains (e.g., EBV strain P3HR1 and in the isolate reported by Sixbey et al. [204], and HHV1 strain HFEM [123, 126]).

The base composition of herpesvirus DNAs varies from 32 to 75 G + C moles/cent (Table 1). Furthermore, herpesvirus DNAs vary with respect to the extent of homogeneity of base sequence distribution along the genome. The extent of inhomogeneity in the base composition varies from minimal (e.g., HSV) to very extensive (e.g., the DNAs of saimirine herpesvirus 2 and ateline herpesvirus 2, see [22]).

An intriguing feature of herpesvirus DNAs is their sequence arrangement. The sequence arrangement shown in Fig. 1 emphasizes the presence and location of reiterations of terminal sequences greater than 100 bp. According to this scheme, the herpesviruses can be divided into six groups designated by the letters A to F. In the genomes of viruses comprising group A and exemplified by the ictalurid herpesvirus 1 (channel catfish herpesvirus), equid herpesvirus 2, and the human herpesvirus 6 (HHV6), a large sequence from one terminus is directly repeated at the other terminus. In the group B genomes exemplified by saimirine herpesvirus 2, the terminal sequence is directly repeated numerous times at both termini; the number of reiterations at both termini may vary. In the group C genomes, exemplified by EBV, the number of direct terminal reiterations is smaller, but there may be other, unrelated, sequences greater than 100 bp that are directly repeated and which subdivide the unique (or quasi unique) sequences of genome into several well delineated stretches. In group D genomes exemplified by those of human herpesvirus 3 (HHV3, varicella zoster virus) and suid herpesvirus 1 (pseudorabies virus), the sequence at one terminus is repeated in an inverted orientation internally. In these genomes, the domain consisting of the stretch of unique sequences flanked by inverted repeats (short or S component) can invert relative to the remaining sequences (long or L component) such that the DNA extracted from virions or infected cells consists of two equimolar populations differing solely in the orientation of the S component relative to the fixed orientation of the L component. In group E viral genomes exemplified by those of HHV1, HHV2, and human herpesvirus 5 (HHV5, human cytomegalovirus), sequences from both termini are repeated in an inverted orientation and juxtaposed internally dividing the genomes into two components, L and S, each of which consists of unique sequences flanked by inverted repeats. In this instance, both

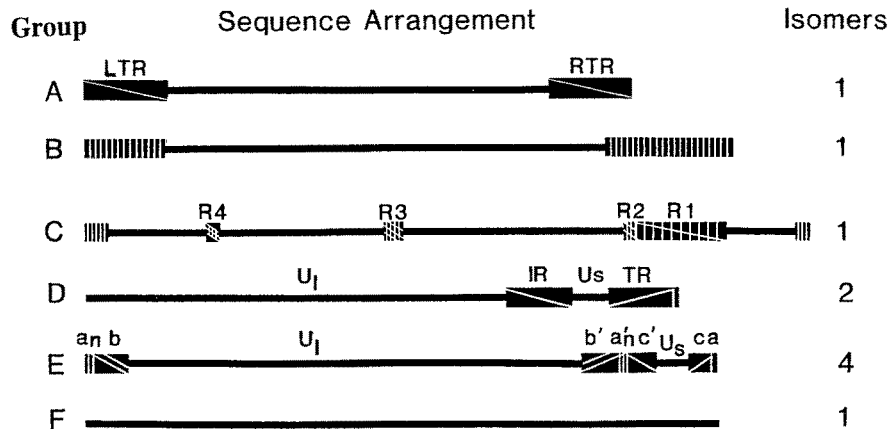


Fig. 1. A schematic diagram of the sequence arrangements in the 6 groups of genomes of the viruses comprising the family *Herpesviridae*. The genomes A, B, C, D, E, and F are exemplified by the ictalurid herpesvirus 1 (channel catfish herpesvirus), saimirine herpesvirus 2 (herpesvirus saimiri), human herpesvirus 4 (EBV), human herpesvirus 3 (VZV), human herpes virus 1 (HSV-1), and tupaiid herpesvirus 1 (tree shrew herpesvirus), respectively. In the schematic diagram the horizontal lines represent unique or quasi-unique regions. The reiterated domains are shown as rectangles and are designated as left and right terminal repeats (*LTR* and *RTR*) for group A, repeats R1 to R4 for internal repeats of group C, and internal and terminal (*IR* and *TR*) repeats of group D. The termini of group E (e.g., HSV) consist of two elements. One terminus contains *n* copies of sequence *a* next to a larger sequence designated as *b*. The other terminus has one directly repeated *a* sequence next to a sequence designated as *c*. The terminal *a_nb* and *ca* sequences are inserted in an inverted orientation (denoted by primes) separating the unique sequences into a long (*U_l*) and short (*U_s*) domains. Terminal reiterations in the genomes of group F have not been described. In group B, the terminal sequences are reiterated numerous times at both termini. The number of reiterations at each terminus may vary. The components of the genomes in groups D and E invert. In group D, the short component inverts relative to the long. Although rarely the long component may also invert, most of the DNA forms two populations differing in the orientation of the short component. In the group E genomes, both the short and long components can invert and viral DNA consists of 4 equimolar isomers.

From [186]

components can invert relative to each other and DNA extracted from virions or infected cells consists of four equimolar populations differing in the relative orientation of the two components. For the genomes comprising the F group exemplified by that of the tupaiid herpesvirus 1 (tupaia herpesvirus), the sequences at the two termini are not identical and are not repeated directly or in an inverted orientation.

Common properties of herpesviruses

The known herpesviruses have been shown to share four significant properties (reviewed in [186]).

(i) All herpesviruses specify enzymes and other factors involved in nucleic acid synthesis metabolism (e.g., DNA polymerase, helicase, primase, origin binding protein, etc.) as well as a variable number of enzymes involved in DNA metabolism (e.g., thymidine kinase, thymidylate synthetase, dUTPase, ribonucleotide reductase, etc.). Herpesviruses specify at least one protease and a variable number of protein kinases.

(ii) The synthesis of viral DNAs and assembly of capsids occur in the nucleus. In the case of some herpesviruses, it has been claimed that the virus may be de-enveloped and re-enveloped as it transits through the cytoplasm. Irrespective of the merits of these conclusions, envelopment of the capsid as it transits through the nuclear membrane is obligatory.

(iii) Production of infectious progeny virus is invariably accompanied by the irreversible destruction of the infected cell.

(iv) The herpesviruses examined to date are able to remain latent in their natural hosts. In cells harboring latent virus, the viral genomes take the form of closed circular molecules and only a small subset of viral genes is expressed.

Distribution in nature

Herpesviruses are widely disseminated in nature, and most animal species have yielded upon examination at least one herpesvirus. Table 1 lists the viruses identified at least on the basis of the architecture of the virus as belonging to the family *Herpesviridae*, and on the basis of serology, analyses of the DNA, or other methods as being a distinct herpesvirus species.

The naming of herpesviruses: definition of species

Summary of the procedure for naming herpesviruses

The procedure for naming herpesviruses is detailed in the 1981 report [187]. Briefly, a formal binomial nomenclature is not currently applied. The herpesviruses are named, with few exceptions, after the latinized name of the *family* of the host which in its natural setting harbors the virus. The exceptions are viruses isolated from humans, nonhuman primates, and from animals of economic importance in which a very large number of herpesviruses has been identified. When more than one virus is isolated from the same host, the viruses are given serial arabic numbers. Thus, herpesviruses isolated from human are designated as "human herpesviruses 1, 2 . . ." etc. Herpesviruses isolated from primates and the family *Bovidae* are designated by subfamily, and the name usually ends in "-ne", as for example, "pongine herpesvirus 1" for the chimpanzee herpesvirus, and "bovine herpesvirus 1" for infectious bovine rhinotracheitis virus. The names of other herpesviruses reflect the host family designation as for example "leporid herpesvirus 1" for the cottontail rabbit herpesvirus. Herpesviruses are numbered in order of discovery, not on the basis of relatedness.

To avoid confusion, if a herpesvirus designated by host family and serial number turns out to belong to another host family or to be a cell culture contaminant, that number is no longer used. In addition, the Herpesvirus Study Group in its 1981 report has specifically recommended against the use of designations such as type, subtype, etc. The Herpesvirus Study Group recognized that common names in use prior to the establishment of these rules will continue to be used.

Naming of herpesviruses implies recognition that the virus represents a new species. In some instances, the differences in the antigenic properties, structure of viral DNAs, and/or host range allow a clear differentiation between different herpesvirus species. For example human herpesviruses 1, 3, 4, and 5 (herpes simplex, varicella zoster, Epstein Barr viruses, and human cytomegaloviruses) are readily differentiated on the basis of antigenic properties, and of differences in base composition, size, sequence arrangement and homology of the DNAs. The HHV1 and HHV2 genomes are closely related and colinear; the viruses arising from recombination events between these two genomes are viable [189]. The basis for considering them as different species are (a) they are readily differentiated by serologic reagents and restriction endonuclease cleavage sites although the genomes of each species are highly polymorphic, and (b) the viruses occupy different ecological niches in that HHV1 generally infects people at a younger age than HHV2 (reviewed in [186, 189, 230]). HHV1

and HHV2 are not the only closely related herpesviruses classified as individual species. Thus a similar basis exists for separation of equid herpesviruses 1 and 4 associated with equine abortion and equine rhinopneumonitis, respectively [194, 217].

A consensus for definition of new species

The Herpesvirus Study Group has purposely avoided defining relatedness on the basis of percent matching of base pairs in as much as in the absence of complete sequences of the genomes the numerical value obtained from such determinations is dependent on experimental design. As a general principle, related viruses could be classified as distinct species if (a) their genomes differ in a readily assayable and distinctive manner across the entire genome (e.g., restriction endonuclease cleavage site patterns obtained with many enzymes) and not merely at a specific site (e.g., small number of genes or small number of restriction endonuclease sites) and (b) if the virus can be shown to have distinct epidemiologic and biologic characteristics. According to this definition, the HHV4 strains differing in the sequence of a small portion of their genome and currently named Epstein-Barr viruses types A and B (EBV-A and EBV-B [120]) would not be designated as distinct species and should be designated as variants A and B. On the other hand, should the HHV6 isolates differing in the patterns of cleavage with numerous restriction endonucleases [200] also differ with respect to epidemiologic and biologic properties, it would be appropriate to designate them as separate species, i.e., as human herpesvirus 6 and 8.

Classification

Current classification

The purpose of classifying viruses into subfamilies and genera is multifold. While a classification scheme is often used to depict evolutionary relatedness, it also serves a practical purpose of enabling the laboratory worker to predict the properties and identity of a new isolate. ICTV has approved the recommendation of its Herpesvirus Study Group that the members of the family *Herpesviridae* be classified initially into 3 subfamilies designated as *Alphaherpesvirinae*, *Betaherpesvirinae*, and *Gammaherpesvirinae*, on the basis of biologic properties in the first instance [187]. The classification is based on the evidence that notwithstanding many shared properties, the herpesviruses also vary greatly in their biologic properties. Some have a wide host species (human or animal) and cell range, multiply efficiently, and rapidly destroy the cells which they infect (e.g., HHV1, HHV2, suid herpesvirus 1, etc.). Others have a narrow host species and cell range (HHV4, HHV6). The multiplication of some herpesvirus appears to be slow (HHV5). While all herpesviruses remain latent in a specific set of cells, the exact cell in which they remain latent varies from one virus to another. For example, whereas latent HHV1 is recovered from sensory neurons, latent HHV4 is recovered from B lymphocytes. Herpesviruses differ with respect to the clinical manifestations of diseases they cause. A summary of the relevant properties of the members of the three subfamilies is as follows.

Alphaherpesvirinae

According to the 1981 proposal herpesviruses included into this subfamily should exhibit nonexclusively a variable host range, relatively short reproductive cycle, rapid spread in culture, efficient destruction of infected cells, and capacity to establish latent infections in sensory ganglia.

Betaherpesvirinae

Nonexclusive characteristics of the members of this subfamily is a restrict host range, a long reproductive cycle and slow spread of infection from cell to cell in culture. The infected cells frequently become enlarged (cytomegalia) and carrier cultures are readily established. The virus can be maintained in latent form in lymphoreticular cells and possibly in secretory glands, kidneys, and other tissues.

Gammaherpesvirinae

The experimental host range of the members of this subfamily is frequently but not exclusively limited to the family or order to which the natural host belongs. In vitro all members replicate in lymphoblastoid cells and some also cause lytic infections in some types of epithelioid and fibroblastic cells. Viruses in this group tend to be specific for either T or B lymphocytes, but exceptions may occur. In the lymphocyte, infection is frequently either at pre-lytic or lytic stage, but frequently without production of infectious progeny. Latent virus is frequently demonstrated in lymphoid tissue.

The ICTV also approved the Herpesvirus Study Group proposals to erect several genera based on DNA sequence homology, similarities in gene and sequence arrangements, and relatedness of important viral proteins demonstrable by immunologic methods (Table 2). While some genes (e.g., glycoprotein B [171, 229] and glycoprotein H [93]), are conserved among members of different subfamilies, nucleic acid and protein sequence homologies of less widely conserved genomic domains are particularly useful for the classification of viruses that are closely related (genera).

Current and future trends in herpesvirus classification

In principle, useful classifications are based on criteria that require a few or simple assays to determine and which are predictive of a whole range of properties and relationships. The biologic criteria used for classification of herpesviruses into subfamilies were based on simple measurements or observations that could be readily determined in numerous laboratories. Fortunately, most herpesviruses assigned to the three subfamilies would have been assigned now to the same subfamilies on the basis of a wider range of objective criteria currently available; indeed, with few exceptions, the criteria proposed in 1981 yielded a scheme of relationships with mirrored that determined since by DNA sequence homology, gene organization, etc. The exceptions, however, are highly significant in that they indicate that the criteria used to align viruses to the three subfamilies are intrinsically unsatisfactory.

The key exceptions are the gallid herpesvirus 1 (GHV1, Marek's disease herpesvirus) classified in 1981 as a member of *Gammaherpesvirinae* and HHV6 which was not known at that time. In nature, GHV1 multiplies and produces cell free, infectious progeny in the keratinized cells of the chicken feather follicles. The virus multiplies in other cells in vivo and in a variety of cell lines in culture, but is retained in cells and not readily released in infectious form. The classification of the virus as a member of the *Gammaherpesvirinae* reflected the observation that the virus caused tumour-like growths in chickens, the tumours were of lymphoid type, and that viral genomes were present and expressed in cells contained in those tumours. Current data indicate that the gene arrangement resembles that of *Alphaherpesvirinae* rather than that of *Gammaherpesvirinae* [38]. It could be argued that the initial classification was erroneous, that it ignored properties which resembled those of *Alphaherpesvirinae* (e.g., growth in fibroblasts, relatively rapid spread in culture notwith-

Table 2. List of genera within the family *Herpesviridae*

Subfamily/ genus	Viruses	Common name
<i>Alphaherpesvirinae</i>		
<i>Simplexvirus</i> ^a	human herpesvirus 1	herpes simplex virus 1
	human herpesvirus 2	herpes simplex virus 2
	bovine herpesvirus 2	bovine mammillitis
	cercopithecine herpesvirus 1	B Virus
<i>Varicellovirus</i> ^a	human herpesvirus 3	varicella-zoster virus
	equid herpesvirus 1	equine abortion virus
	bovine herpesvirus 1	infectious bovine rhinotracheitis virus
	suid herpesvirus 1	pseudorabies virus
<i>Betaherpesvirinae</i>		
<i>Cytomegalovirus</i> ^a	human herpesvirus 5	human cytomegalovirus
<i>Muromegalovirus</i> ^a	murid herpesvirus 1	murine cytomegalovirus
<i>Roseolovirus</i> ^b	human herpesvirus 6	
	human herpesvirus 7	
<i>Gammaherpesvirinae</i>		
<i>Lymphocryptovirus</i> ^a	human herpesvirus 4	Epstein-Barr Virus
	cercopithecine herpesvirus 12	baboon herpesvirus
	cercopithecine herpesvirus 14	African green monkey, EBV like virus
	cercopithecine herpesvirus 15	rhesus monkey EBV like virus
	pongine herpesvirus 1	chimpanzee herpesvirus
	pongine herpesvirus 2	orangutan herpesvirus
	pongine herpesvirus 3	gorilla herpesvirus
	ateline herpesvirus 2	herpesvirus ateles 2
	saimirine herpesvirus 2	herpesvirus saimiri 2
	bovine herpesvirus 2	
<i>Rhadinovirus</i> ^a	alcelaphine herpesvirus 1	virus of malignant catharral fever
	murid herpesvirus 1	mouse herpesvirus strain 68

^a Approved by International Committee on Taxonomy of Viruses

^b Proposed name for genus

standing its cell associatedness, etc.) and took into account the one criterion which was not among those listed for classification, namely that none of the known viruses which comprise the *Alphaherpesvirinae* commonly cause tumours in their natural hosts and remain associated with the tumour cells.

The ambiguity which surrounds the initial classification of GHV1 as a *Gammaherpesvirus* is less apparent in the case of HHV6. By the 1981 criteria, HHV6 should be assigned to the *Gammaherpesvirinae* on the basis of its tropism for lymphocytes. However, on the basis of sequence homology and gene organization, HHV6 is related to HHV5 and more properly belongs to the *Betaherpesvirinae*. It is worth noting that lymphocytes are fully permissive to HHV6 whereas gammaherpesviruses generally cause non-productive or latent infection in this cell type. Our knowledge of the biology of HHV5 has also undergone a change in that we are not as likely to exclude the association of this virus with lymphoid cells as was the case in 1981.

The problem now facing the Herpesvirus Study Group is the selection of objective criteria that match the 1981 criteria in simplicity and usefulness, but lack the ambiguity to

which the 1981 criteria are subject. The objective criteria that have been proposed for the classification of herpesvirus subfamilies are (i) conservation of genes and gene clusters (e.g., DNA polymerase, glycoproteins B, C, and H, single strand DNA binding protein, major capsid protein, etc.) (ii) the arrangement of gene clusters relative to each other; (iii) the arrangement of the terminal sequences involved in packaging of the viral genome; and (iv) the presence and distribution of nucleotides that are subject to methylation [42, 56, 58, 60, 92, 125, 167].

The selection of suitable criteria depends on the purpose for collecting taxonomic data. The objectives of herpesvirus taxonomy are multifold. At one level, the taxonomy must provide a quantitative measure of the relatedness of the different herpesviruses to each other from which one can infer an evolutionary tree. At the other extreme, not all herpesviruses rampant in nature have been identified and taxonomy must also serve the purely utilitarian function of assisting those involved in the isolation of new viruses to predict biologic properties in the same fashion that anatomic characteristic serve to identify insects and plants and biochemical and morphologic properties identify bacteria.

Taxonomic data useful for the erection of an evolutionary tree must be based on nucleotide sequence of viral genomes. At present the sequence of at least 10 herpesviruses is either known or nearing completion (e.g., HHV1-6, saimirine herpesvirus 2, equine herpesvirus 1, and ictalurid herpesvirus 1). Although additional herpesvirus genomes are likely to be sequenced, it is not likely that the number of genomes analyzed in this fashion will keep pace with the discovery of new herpesviruses. On the other hand, although the number of sequenced herpesvirus genomes represents less than 10% of the known herpesviruses, the data generated from this collection may suggest limited domains of other herpesviruses which must be sequenced to place them in the appropriate taxonomic groups. The central question is the nature of these domains. A more complex problem is the identification of nucleotide or protein sequence correlates of biologic properties of the various herpesviruses.

At present arguments can be marshalled to reject each of the criteria proposed to date, and a few examples may suffice. For example, it can be argued that highly conserved genes are responsible for the common properties of herpesviruses, and hence analyses of the sequence of their products might provide clues to their evolutionary relationships. Inasmuch as the object of the taxonomy of herpesviruses is to differentiate among a family of viruses which share very obvious structural and replicative properties and yet show considerable biologic diversity, the key question is whether evolutionary divergence of the conserved genes could be prognostic of biologic diversity.

Another proposal enumerated above centered on the polarity and colinearity of conserved gene clusters. The argument is that such arrangements are likely to have evolved gradually and may reflect evolutionary relationship more precisely than gene product sequence which might be under selective pressure imposed by the ecological niche of the virus. The counter argument is that gene rearrangements arise through intermolecular and intramolecular inversion and recombination events that are known to occur among herpesviruses and that such arrangements while useful in defining potential relationships may not arise solely by divergent evolution and also may not be prognostic of biologic properties.

It can be argued also that each herpesvirus occupies a unique ecologic niche and that the genes prognostic of biologic diversity are genes unique to specific ecologic niches, i.e., replicating or remaining latent in specific cells or organs, but not conserved among all herpesviruses. Such genes could be predicted to be dispensable for growth of cells in culture.

The size of this group of genes is reflected in the observation that 38 of the 73 diverse open reading frames of HHV1 can be deleted without abolishing the capacity of the virus to multiply at least in some cells in culture ([189] and B. Roizman, unpubl. data). The function of these deletable genes is largely unknown, and most of them are not conserved across different subfamilies. To illustrate the point in the context of GHV1, the conserved genes, i.e., those that are homologous and nearly colinear with those of HHV3 [38] are not the domains expressed during latency or in transformed cells. The expression of GHV1 in cells harboring latent virus is quite different from that of HHV3 [218]. Delineation and evolutionary relatedness of genes responsible for biologic properties may be a more significant criterion for both evolutionary relatedness and classification than the arrangement and evolution of genes conserved throughout the family *Herpesviridae*. The problems with this approach are also numerous. Not all “dispensable” or non conserved genes are necessarily prognostic of biologic activity and the function of most of the non conserved genes is not known.

The present position of the Herpesvirus Study Group is as follows: (i) Nucleotide sequence data are necessarily the basis of the taxonomy of the family *Herpesviridae*. The central issue is the identification of the correlates which must be culled from such data for a truly useful taxonomy. (ii) The Study Group as well as the herpesvirus community is confronted with a large number of options which may eventually lead to the construction of an evolutionary tree, but none provide as yet clear correlates between predicted herpesvirus protein sequence and biologic properties. (iii) No single property is likely to form the basis of a truly useful and enduring taxonomy of herpesvirus. The key properties which jointly are likely to form the basis of a future taxonomy are the evolutionary divergence of conserved genes, the identification of nonconserved genes that best correlate with the ecologic niches of the diverse herpesviruses, and the gene polarity and clustering within the viral genomes. The exponential increase in the generation of data on herpesviruses suggests that the information required for a taxonomy based on more objective criteria than the one currently available may not be long in coming.

References

1. Ablashi DV, Chopra HC, Armstrong GR (1972) A cytomegalovirus isolated from an owl monkey. *Lab Anim Sci* 22: 190-195
2. Allen GP, Bryans JT (1986) Molecular epizootiology, pathogenesis and prophylaxis of equine herpesvirus 1 infections. *Prog Vet Microbiol Immunol* 2: 78-144
3. Armstrong JA, Pereira HG, Andrewes CH (1961) Observation of the virus of infectious bovine rhinotracheitis and its affinity with the herpesvirus group. *Virology* 14: 276-285
4. Asher Y, Heller M, Becker Y (1969) Incorporation of lipids into herpes simplex virus particles. *J Gen Virol* 4: 65-76
5. Asher DM, Gibbs CJ, Long DJ (1969) Rhesus monkey cytomegalovirus: persistent asymptomatic viraemia. *Bacteriol Proc Abstract* V269
6. Baer R, Bankier AT, Biggin MD, Deininger PL, Farrell PJ, Gibson TG, Hatfull G, Hudson GS, Satchwell SC, Seguin C, Tuffnell PS, Barrell BG (1984) DNA sequence and expression of the B95-8 Epstein-Barr virus genome. *Nature* 310: 207-211
7. Barahona HH, Daniel MD, Katz SL, Ingalls JK, Melendez LV, King NW (1975) Isolation and in vitro characterization of a herpesvirus from ground squirrels (*Citellus* sp). *Lab Anim Sci* 25: 725-739
8. Barahona HH, Trum BF, Melendez LV, Garcia FG, King NW, Daniel MD, Jackman DA (1973) A new herpes virus isolated from kinkajou (*Botos flavus*). *Lab Anim Sci* 23: 830-836
9. Bartha A, Juhasz M, Liebermann H (1966) Isolation of a bovine herpesvirus from calves with respiratory disease and keratoconjunctivitis. *Acta Vet Acad Sci* 16: 357-358
10. Basson PA, McCully RM, DeVoss B, Young E, Schulze P (1971) Some parasitic and other natural diseases of the African elephant in the Kruger National Park. *Onderstepoort J Vet Res* 38: 239-254

11. Baudet AETF (1928) Mortality in ducks in the Netherlands caused by a filterable virus: fowl plague. *Tijdschr Diergeneeskde* 50: 455–459
12. Ben-Porat T, Kaplan AS (1971) Phospholipid metabolism of herpesvirus-infected and uninfected rabbit kidney cells. *Virology* 45: 252–264
13. Ben-Porat T, Kaplan AS (1985) Molecular biology of pseudorabies virus. In: Roizman B (ed) *The herpesviruses*, vol 3. Plenum, New York, pp 105–173
14. Berezsky IK, Grimley PM, Tyrell SA (1971) Ultrastructure of a rat cytomegalovirus. *Exp Mol Pathol* 14: 337–349
15. Bhatt PN, Percy DH, Craft JL, Jonas AM (1971) Isolation and characterization of a herpes-like (Hsiung-Kaplow) virus from guinea pigs. *J Infect Dis* 123: 178–179
16. Bia FJ, Summers WC, Fong CKY, Hsiung GD (1980) New endogenous herpesvirus of guinea pigs: biological and molecular characterization. *J Virol* 36: 245–253
17. Black PH, Hartley J, Rowe WP (1963) Isolation of cytomegalovirus from African green monkey. *Proc Soc Exp Biol Med* 112: 601–605
18. Blakely GA, Lourie B, Morton WG, Evans HH, Kaufman AF (1973) A varicella-like disease in macaque monkeys. *J Infect Dis* 127: 617–625
19. Blaskovic D, Stancekova M, Svobodova J, Kresakova J (1980) Isolation of five strains of herpesvirus from two species of free living small rodents. *Acta Virol* 24: 468
20. Blaskovic D, Sekayova Z, Turna J, Kudelova M, Slavik J, Mucha V (1988) Purification of murine alpha-herpesvirus and some properties of its DNA. *Acta Virol* 32: 329–333
21. Bocker JF, Tiedemann K-H, Bornkamm GW, Zur Hausen M (1980) Characterization of an EBV-like virus from African green monkey lymphoblasts. *Virology* 101: 291–295
22. Bornkamm GW, Delius H, Fleckenstein B, Werner FJ, Mulder C (1976) Structure of herpes saimiri genomes: arrangement of heavy and light sequences in the M genome. *J Virol* 19: 154–161
23. Borst GHA, Walvoort HC, Reijnders PJH, Van der Kamp JS, Osterhaus ADME (1986) An outbreak of a herpesvirus infection in harbor seals (*Phoca vitulina*). *J Wildl Dis* 22: 1–6
24. Brake F, Studdert MJ (1985) Molecular epidemiology and pathogenesis of ruminant herpesviruses including bovine, buffalo, and caprine herpesvirus 1 and bovine encephalitis herpesvirus. *Aust Vet J* 62: 331–334
25. Breese SS Jr, Dardiri AH (1968) Electron microscopic characterization of duck plague virus. *Virology* 34: 160–169
26. Bridgen A (1991) The derivation of a restriction endonuclease map for alcelaphine herpesvirus 1 DNA. *Arch Virol* 117: 183–192
27. Bridgen A, Herring AJ, Inglis NF, Reid HW (1989) Preliminary characterization of the alcelaphine herpesvirus 1 genome. *J Gen Virol* 70: 1141–1150
28. Bridgen A, Reid HW (1991) Deviation of a DNA clone corresponding to the viral agent of sheep-associated malignant catarrhal fever. *Res Vet Sci* 50: 38–44
29. Browning GF, Ficorilli N, Studdert MJ (1988) Asinine herpesvirus genomes: comparison with those of the equine herpesviruses. *Arch Virol* 101: 183–190
30. Browning GF, Studdert MJ (1987) Genomic heterogeneity of equine betaherpesviruses. *J Gen Virol* 68: 1441–1447
31. Browning GF, Studdert MJ (1989) Physical mapping of a genome of equine herpesvirus 2 (equine cytomegalovirus). *Arch Virol* 104: 77–86
32. Browning GF, Studdert MJ (1989) Physical mapping of the genomic heterogeneity of isolates of equine herpesvirus 2 (equine cytomegalovirus). *Arch Virol* 104: 87–94
33. Bublot M, Van Bressen M, Thiry E, Dubuisson J, Pastoret P (1990) Bovine herpesvirus 4 genomes: cloning, mapping, and strain variation analysis. *J Gen Virol* 71: 133–142
34. Bublot M, Dubuisson M-F, Van Bresse SD, Pastoret P-P, Thiry E (1991) Antigenic and genomic identity between simian herpesvirus aotus type 2 and bovine herpesvirus type 4. *J Gen Virol* 72: 715–719
35. Buchanan JS, Richards RH, Sommerville C, Madeley CR (1978) A herpestype virus from turbot (*Scophthalmus maximus* L). *Vet Rec* 102: 527–528
36. Buchman TG, Roizman B (1978) Anatomy of bovine mammillitis virus DNA. I. Restriction endonuclease maps of four populations of molecules that differ in the relative orientation of their long and short components. *J Virol* 25: 395–407
37. Buchman TG, Roizman B (1978) Anatomy of bovine mammillitis DNA. II. Size and arrangements of the deoxynucleotide sequences. *J Virol* 27: 239–254
38. Buckmaster AE, Scott SD, Sanderson MJS, Bournnell MEG, Ross NLJ, Binns MM (1988) Gene sequence

- and mapping data from Marek's disease virus and herpesvirus of turkeys: Implications for herpesvirus classification. *J Gen Virol* 69: 2033–2042
39. Bülow VV, Biggs PM (1975) Differentiation between strains of Marek's disease virus and turkey herpesvirus by immuno-fluorescence assays. *Avian Pathol* 4: 133–145
 40. Bürki F, Burtscher H, Sibalin M (1973) Herpesvirus strigis: a new avian herpesvirus. I. Biological properties. *Arch Ges Virusforsch* 43: 14–24
 41. Burtscher H, Grunberg W (1979) Herpesvirus-Hepatitis bei Kranichen (Aves-Gruidae). I. Pathomorphologische Befunde. *Zentralbl Veterinaermed [B]* 26: 561–569
 42. Cameron KR, Stamminger T, Craxton M, Bodemer W, Honess RW, Fleckenstein B (1987) The 160,000 M_r virion protein encoded at the right end of the herpesvirus saimiri genome is homologous to the 140,000 M_r membrane antigen encoded at the left end of the Epstein-Barr virus genome. *J Virol* 61: 2063–2070
 43. Cebrian J, Bucchini D, Sheldrick P (1983) Endless viral DNA in cells infected with channel catfish virus. *J Virol* 46: 405–412
 44. Cebrian J, Kaschka-Dierich C, Berthelot N, and Sheldrick P (1982) Inverted repeat nucleotide sequences in the genomes of Marek's disease virus and the herpesvirus of the turkey. *Proc Natl Acad Sci USA* 79: 555–558
 45. Chee MS, Bankier AT, Beck S, Bohni R, Brown CM, Cerny R, Horsnell T, Hutchinson III CA, Kouzarides T, Martignetti JA, Preddie E, Satchwell SC, Tomlinson P, Weston KM, Barrell BG (1990) Analysis of the protein-coding content of the sequence of human cytomegalovirus strain AD169. *Curr Top Microbiol Immunol* 154: 125–169
 46. Chousterman S, Lacasa M, Sheldrick P (1979) Physical map of the channel catfish virus genome: location of sites for restriction endonucleases *EcoRI*, *HindIII*, *HpaI*, and *XbaI*. *J Virol* 37: 73–85
 47. Churchill AE, Biggs PM (1967) Agent of Marek's disease in tissue culture. *Nature* 215: 528–530
 48. Clark HF, Karzon DT (1972) Iguana virus, a herpes-like virus isolated from cultured cells of a lizard, *Iguana iguana*. *Infect Immun* 5: 559–569
 49. Clarkson MJ, Thorpe E, McCarthy K (1967) A virus disease of captive vervet monkeys (*Cercopithecus aethiops*) caused by a new herpesvirus. *Arch Ges Virusforsch* 22: 219–234
 50. Cornwell HJC, Wright NG, McCusker HB (1970) Herpesvirus infection of pigeons. II. Experimental infection of pigeons and chicks. *J Comp Pathol* 80: 229–232
 51. Cox WR, Rapley WA, Barker IK (1980) Herpesvirus-like infection in the painted turtle (*Chrysemys picta*). *J Wildl Dis* 16: 445–449
 52. Cruickshank JO, Berry DM, Hay B (1963) The fine structure of infectious laryngotracheitis virus. *J Virol* 20: 376–378
 53. Cullinane AA, Rixon FJ, Davison AJ (1988) Characterization of the genome of equine herpesvirus 1 subtype 2. *J Gen Virol* 69: 1575–1590
 54. Daniel MD, Melendez LV, King NW, Fraser CEO, Barahona HH, Hunt RD, Garcia FG (1971) Herpes virus aotus: a latent herpesvirus from owl monkeys (*Aotus trivirgatus*). Isolation and characteristics. *Proc Soc Exp Biol Med* 138: 835–845
 55. Darai G, Matz B, Schroder CH, Flugel RH, Berger U, Munk K, Gelderblom H (1979) Characterization of a tree shrew herpesvirus isolated from a lymphosarcoma. *J Gen Virol* 43: 541–551
 56. Davison AJ, McGeoch DJ (1986) Evolutionary comparisons of the S segments in the genomes of herpes simplex virus type 1 and varicella-zoster virus. *J Gen Virol* 67: 597–611
 57. Davison AJ, Scott JE (1986) The complete DNA sequence of varicella-zoster virus. *J Gen Virol* 67: 1759–1816
 58. Davison AJ, Taylor P (1986) Genetic relations between varicella-zoster virus and Epstein-Barr virus. *J Gen Virol* 68: 1067–1079
 59. Deinhardt F, Falk LA, Wolfe LG (1973) Simian herpesviruses. *Cancer Res* 33: 1424–1426
 60. Deiss LP, Chou J, Frenkel N (1986) Functional domains with the a sequence involved in the cleavage-packaging of herpes simplex virus DNA. *J Virol* 59: 605–618
 61. De Villiers EM, Els HJ, Verwoerd DW (1975) Characteristics of an ovine herpesvirus associated with pulmonary adenomatosis (jaagsiekte) in sheep. *S Afr J Med Sci* 40: 165–170
 62. De Villiers EM (1979) Purification of the JS-3 isolate of herpesvirus ovis (bovid herpesvirus 4) and some properties of its DNA. *J Virol* 32: 705–709
 63. Diosi P, Babusceac L, David C (1967) Recovery of cytomegalovirus from the submaxillary glands of ground squirrels. *Arch Ges Virusforsch* 20: 383–386
 64. Diosi P, Plavosin L, Arcan P, David C (1975) Recovery of a new herpesvirus form the ground squirrel. *Pathol Microbiol* 42: 42–48

65. Ditchfield J, Grinyer I (1965) Feline rhinotracheitis virus: a feline herpesvirus. *Virology* 26: 504–506
66. Docherty DE, Romaine RI, Knight RL (1983) Isolation of a herpesvirus from a bald eagle nesting. *Avian Dis* 27: 1162–1165
67. Dubuisson J, Danyi S, Bublot M, Pastoret P-P, Thiry E (1991) Comparison of proteins of simian aotus type 2 and bovine herpesvirus 4. *J Gen Virol* 72: 1145–1150
68. Dumas AM, Geelen JLMC, Maris W, Van der Noordaa J (1980) Infectivity and molecular weight of varicella-zoster virus DNA. *J Gen Virol* 47: 233–235
69. Ebeling A, Keil G, Nowak B, Fleckenstein B, Berthelot N, Sheldrick P (1983) Genome structure and virion polypeptides of the primate herpesviruses, *Herpesvirus aotus* types 1 and 3; comparison with human cytomegalovirus. *J Virol* 45: 715–726
70. Ebeling A, Keil GM, Knust E, Koszinowski UH (1983) Molecular cloning and physical mapping of murine cytomegalovirus DNA. *J Virol* 47: 421–433
71. Efstathiou S, Ho YM, Minson AC (1990) Cloning and molecular characterization of the murine herpesvirus 68 genome. *J Gen Virol* 71: 1355–1364
72. Ek-Kommonen C, Pelkonen S, Nettleton PF (1986) Isolation of herpesvirus serologically related to bovine herpesvirus 1 from a reindeer (*Rangifer tarandus*). *Acta Vet Scand* 27: 299–301
73. Engles M, Giuliani C, Wild P, Beck TM, Loepfe E, Wyler R (1986) The genome of bovine herpesvirus 1 (BHV-1) strains exhibiting a neuropathogenic potential compared to known BHV-1 strains by restriction site mapping and cross hybridization. *Virus Res* 6: 57–73
74. Engles M, Loepfe E, Wild P, Schraner E, Wyler R (1987) The genome of caprine herpesvirus 1: genome structure and relatedness to bovine herpesvirus 1. *J Gen Virol* 68: 2019–2023
75. Epstein MA (1962) Observations on the fine structure of mature herpes simplex virus and on the composition of its nucleoid. *J Exp Med* 115: 1–12
76. Epstein MA, Henle W, Achong BG, Barr YM (1965) Morphological and biological studies on virus in cultured lymphoblasts from Burkitt's lymphoma. *J Exp Med* 121: 761–770
77. Falk L, Deinhardt F, Nonoyama M, Wolfe LG, Bergholz C, Lapin B, Yakovleva L, Agrba V, Henle G, Henle W (1976) Properties of a baboon lymphotropic herpesvirus related to Epstein-Barr virus. *Int J Cancer* 18: 798–807
78. Falke D, Siegert R, Vogell W (1959) Elektronenmikroskopische Befunde zur Frage der Doppelmembranbildung des Herpes-simplex-Virus. *Arch Ges Virusforsch* 9: 484–496
79. Fleckenstein B, Bornkamm GW, Mulder C, Werner F-J, Daniel MD, Falk LA, Delius H (1978) Herpesvirus ateles DNA and its homology with herpesvirus saimiri nucleic acid. *J Virol* 25: 361–373
80. Fleckenstein B, Desrosiers RC (1982) Herpesvirus saimiri and herpesvirus ateles. In: Roizman B (ed) *The herpesviruses*, vol 1. Plenum, New York, pp 253–332
81. Fong CKY, Tenser RB, Hsiung GD, Gross PA (1973) Ultrastructural studies of the envelopment and release of guinea pig herpeslike virus in cultured cells. *Virology* 52: 468–477
82. Frye FL, Oshiro LO, Dutra FR, Carney JD (1977) Herpesvirus-like infection in two Pacific pond turtles. *J Am Vet Med Assoc* 171: 882–884
83. Fukuchi K, Sudo M, Lee Y-S, Tanaka A, Nonoyama M (1984) Structure of Marek's disease DNA: detailed restriction enzyme map. *J Virol* 102–109
84. Furlong D, Swift H, Roizman B (1972) Arrangement of herpesvirus deoxyribonucleic acid in the core. *J Virol* 10: 1071–1074
85. Frank AL, Bissell JA, Rowe DS, Dunnick NR, Mayner RE, Hopps HE, Parkman PD, Meyer HM Jr (1973) Rhesus leucocyte-associated herpesvirus. I. Isolation and characterization of a new herpesvirus recovered from rhesus monkey leukocytes. *J Infect Dis* 128: 618–629
86. French EL (1961) Relationship between infectious bovine rhinotracheitis (IBR) virus and a virus isolated from calves with encephalitis. *Aust Vet J* 38: 555–556
87. French EL, Purchase HG, Nazerian K (1973) A new herpesvirus isolated from a nestling cormorant (*Phalacrocorax melanoleucos*). *Avian Pathol* 2: 3–15
88. Frenkel N, Schirmer EC, Wyatt LS, Katsafanas G, Roffman E, Danovich RM, June CH (1990) Isolation of a new herpesvirus from human CD4⁺ T cells. *Proc Natl Acad Sci USA* 87: 748–752
89. Gelb LD (1990) Varicella-zoster virus. In: Fields BN, Knipe DM (eds) *Fields' virology*, vol 2, 2nd edn. Raven Press, New York, pp 2011–2054
90. Gibbs EPJ, Rweyemamu MM (1977) Bovine herpesviruses. *Vet Bull* 47: 317–425
91. Gilles NG, Ogstron CW (1991) Structure and expression of the woodchuck herpesvirus genome. *Virology* 180: 434–438

92. Gompels UA, Craxton MA, Honess RW (1988) Conservation of gene organization in the lymphotropic herpesviruses herpesvirus saimiri and Epstein-Barr virus. *J Virol* 62: 757-767
93. Gompels UA, Craxton MA, Honess RW (1988) Conservation of glycoprotein H (gH) in herpesviruses: nucleotide sequence of the gH gene from herpesvirus saimiri. *J Gen Virol* 69: 2819-2829
94. Goodheart C, Plummer G (1974) The densities of herpes viral DNAs. *Prog Med Virol* 19: 324
95. Gravell M (1971) Viruses and renal carcinoma of *Rana pipiens*. X. Comparison of herpes type viruses associated with Lucké tumour-bearing frogs. *Virology* 43: 730-733
96. Gruter W (1924) Das Herpesvirus, seine aetiologische und klinische Bedeutung. *Muench Med Wochenschr* 71: 1058-1060
97. Gustafson DP (1986) Pseudorabies. In: Leman AD (ed) *Diseases of swine*, 6th edn. Iowa State University Press, Ames, pp 274-289
98. Haines H, Kleese WC (1977) Effect of water temperatures on a herpesvirus infection of sea turtles. *Infect Immun* 15: 756-759
99. Hamparian VV, Hilleman MR, Ketler A (1963) Contributions to characterization and classification of animal viruses. *Proc Soc Exp Biol Med* 112: 1040-1052
100. Hartley HW, Rowe WP, Huebner RJ (1971) Serial propagation of the guinea pig salivary gland virus in tissue culture. *Proc Soc Exp Biol Med* 96: 281-285
101. Hauser B, Mettler F, Rubel A (1983) Herpes-like infection in two young boas. *J Comp Pathol* 93: 515-519
102. Heller M, Gerber P, Kieff E (1982) DNA of herpesvirus PAN, a third member of the Epstein-Barr virus-herpesvirus papio group. *J Virol* 41: 931-939
103. Heller M, Kieff ED (1981) Colinearity between the DNAs of Epstein-Barr virus and herpes virus papio. *J Virol* 37: 698-709
104. Hinze HC (1971) New member of the herpesvirus group isolated from wild cottontail rabbits. *Infect Immun* 3: 350-354
105. Holmes AW, Caldwell RG, Dedmon RE, Deinhardt F (1964) Isolation and characterization of a new herpes virus. *J Immunol* 92: 602-610
106. Honess RW, Gompels UA, Barrell BG, Craxton M, Cameron KR, Staden R, Chang Y-N, Hayward GS (1989) Deviations from expected frequencies of CpG dinucleotides in herpesvirus DNAs may be diagnostic of differences in the states of their latent genomes. *J Gen Virol* 70: 837-855
107. Hsiung GD, Kaplow LS (1969) Herpes like virus isolated from spontaneously degenerated tissue culture derived from leukemia-susceptible guinea pigs. *J Virol* 3: 355-357
108. Hull RN, Dwyer AC, Holmes AW, Nowakowski E, Deinhardt F, Lennette EH, Emmons RW (1972) Recovery and characterization of a new simian herpesvirus from a fatally infected spider monkey. *J Natl Cancer Inst* 49: 225-230
109. Inglis DM, Bowie JM, Allan MJ, Nettleton PF (1983) Ocular disease in red deer calves associated with a herpesvirus infection. *Vet Rec* 113: 182-183
110. Jackman DA, King NW, Daniel MD, Sehgal DK, Fraser CEO (1977) *M. cyclopis*: a new herpesvirus isolated from *Macaca cyclopis*. In: Abstracts of the Annual Meeting of the American Society for Microbiology, V348
111. Jacob RJ, Cohen D, Bouchey D, Davis T, Borchelt J (1988) Molecular pathogenesis of equine coital exanthema a new equine herpesvirus isolated from lesions reminiscent of coital exanthema in a donkey. In: Powell DG (ed) *Equine infectious diseases V*. The University of Kentucky Press, Lexington, pp 140-146
112. Jacobson ER, Clubb S, Gaskin JM, Gardner C (1985) Herpesvirus like infection in Argentine tortoises. *J Am Vet Med Assoc* 187: 1227-1229
113. Jacobson ER, Gaskin JM, Wahlquist H (1982) Herpes-like infection in map turtles. *Am J Vet Res* 181: 1322-1324
114. Johnson MA, Whalley JM (1987) Restriction enzyme maps of the macropodid herpesvirus 2 genome. *Arch Virol* 96: 153-168
115. Johnson MA, Whalley JM, Littlejohns IR, Dickson J, Smith VW, Wilks CR, Reisner AH (1985) Macropodid herpesviruses 1 and 2: two herpesviruses from Australian marsupials differentiated by restriction endonucleases, DNA composition and hybridization. *Arch Virol* 85: 313-319
116. Kaleta EF, Marschall HJ, Glunder G, Stiburek B (1980) Isolation and serological differentiation of a herpesvirus from bobwhite quail (*Colinus virginianus*, L. 1758). *Arch Virol* 66: 359-364
117. Kaleta EF, Mikami T, Marschall HJ, Heffels U, Heidenreich M, Stiburek B (1980) A new herpesvirus isolated from black storks (*Ciconia nigra*). *Avian Pathol* 9: 301-310
118. Kawamura H, King DJ, Anderson DP (1969) A herpesvirus isolated from kidney cell culture of normal turkeys. *Avian Dis* 13: 853-863

119. Kelly RK, Nielsen O, Yamamoto T (1980) A new herpes-like virus (HLV) of fish (*Stizostedion vitreum-vitreum*). In Vitro 16: 225
120. Kieff E, Liebowitz D (1990) Epstein-Barr virus and its replication. In: Fields BN, Knipe DM et al (eds) Fields' virology, vol 2, 2nd edn. Raven Press, New York, pp 1889–1920
121. Kimura T, Ioshimizu M, Tanaka M (1980) Salmonid viruses: effect of *Oncorhynchus mason virus* (OMV) in fry of chum salmon (*Oncorhynchus keta*). Fish Health News 9: 2–3
122. Kincaid AL, Bunton TE, Cranfield M (1988) Herpes-like infection in black-footed penguins (*Spheniscus demersus*). J Wildl Dis 24: 173–175
123. Knipe DM, Ruyechan WT, Roizman B, Halliburton IW (1978) Molecular genetics of herpes simplex virus: demonstration of regions of obligatory and nonobligatory identity within diploid regions of the genome by sequence replacement and insertion. Proc Natl Acad Sci USA 75: 3896–3900
124. Koch H-G, Delius H, Matz B, Flugel RM, Clarke J, Darai G (1985) Molecular cloning and physical mapping of the tupaia herpesvirus genome. J Virol 55: 86–95
125. Kouzarides T, Bankier AT, Satchwell SC, Weston K, Tomlinson P, Barrell BG (1987) Large scale rearrangements of homologous regions in the genomes of HCMV and EBV. Virology 157: 397–413
126. Koch H-G, Rosen A, Ernst F, Becker Y, Darai G (1987) Determination of the nucleotide sequence flanking the deletion (0.762 and 0.789 map units) in the genome of an intraperitoneally avirulent HSV-1 strain HFEM. Virus Res 7: 105–115
127. Landon JE, Ellis LB, Zeve VH, Fabrizio DP (1968) Herpes-type virus in cultured leukocytes from chimpanzees. J Natl Cancer Inst 40: 181–192
128. L'Ecuyer C, Corner AH (1966) Propagation of porcine cytomegalic inclusion disease virus in cell cultures: preliminary report. Can J Comp Med Vet Sci 30: 321–326
129. Lee LF, Armstrong RL, Nazerian K (1972) Comparative studies of six avian herpesviruses. Avian Dis 16: 799–805
130. Leib DA, Bradbury JM, Hart CA, McCarthy K (1987) Genome isomerism in two alphaherpesviruses: Herpesvirus saimiri-1 (herpesvirus tamarinus) and avian infectious laryngotracheitis virus. Arch Virol 93: 287–294
131. Lewis MA, Frye LD, Gibbs CJ Jr, Chou SM, Cutchins EC, Gajdusek DC, Ward G (1976) Isolation and characterization of two new herpes-like viruses from Capuchin monkeys. Infect Immun 14: 759–766
132. Lindquister GJ, Pellett PE (1991) Properties of the human herpesvirus 6 strain Z29 genome: G + C content, length, and the presence of variable-length repeated terminal sequence elements. Virology 182: 102–110
133. Lopez C, Honess RW (1990) Human herpesvirus-6. In: Fields BN, Knipe DM et al (eds) Fields' virology, vol 2, 2nd edn. Raven Press, New York, pp 2055–2075
134. Lopez C, Pellett P, Stewart J, Goldsmith C, Sanderlin K, Black J, Warfield D, Feorino P (1988) Characteristics of human herpesvirus-6. J Infect Dis 157: 1271–1273
135. Lucke B (1938) Carcinoma of the leopard frog: its probable causation by a virus. J Exp Med 68: 457–466
136. Ludwig H, Biswal N, Bryans JT, McCombs RM (1971) Some properties of the DNA from a new equine herpesvirus. Virology 45: 534–537
137. Lunger PD, Clark HF (1978) Reptilia-related viruses. Adv Virus Res 23: 159–204
138. MacKay JMK (1969) Tissue culture studies of sheep pulmonary adenomatosis (Jaagsiekte). I. Direct culture of affected lungs. J Comp Pathol 79: 141–146
139. Madin SH, York CJ, McKercher DG (1956) Isolation of the infectious bovine rhinotracheitis virus. Science 124: 721–722
140. Malherbe M, Harwin R, Ulrich M (1963) The cytopathic effects of vervet monkey viruses. S Afr Med J 37: 407–411
141. Mare CJ, Graham DL (1973) Falcon herpesvirus, the etiologic agent of inclusion body disease of falcons. Infect Immun 8: 118–126
142. Martin MED, Thomson BJ, Honess RW, Craxton MA, Gompels UA, Liu M-Y, Littler E, Arrand JR, Teo I, Jones MD (1991) The genome of human herpesvirus 6: maps of unit-length and concatemeric genomes for nine restriction endonucleases. J Gen Virol 72: 157–168
143. Martin WB, Hay D, Crawford LV, Lebouvier GL, Crawford EM (1966) Characteristics of bovine mammillitis virus. J Gen Microbiol 45: 325–332
144. May HG, Tittsler RP (1925) Tracheo-laryngitis in poultry. J Am Vet Med Assoc 67: 229–231
145. Mayfield JE, Good PJ, van Oort HJ, Campbell AR, Reed DE (1983) Cloning and cleavage site mapping of DNA from bovine herpesvirus 1 (Cooper strain). J Virol 47: 259–264
146. McCarthy K, Thorpe E, Laursen AC, Heymann CS, Beale JA (1968) Exanthematous disease in patas monkeys caused by a herpes virus. Lancet 2: 856–857

147. McCombs R, Brunschwig JP, Mirkovic R, Benyesh-Melnick M (1971) Electron microscopic characterization of a herpes-like virus isolated from tree shrews. *Virology* 45: 816–820
148. McGeoch DJ, Dalrymple MA, Davison AJ, Dolan A, Frame MC, McNab D, Perry LJ, Scott JE, Taylor P (1988) The complete DNA sequence of the long unique region in the genome of herpes simplex virus type 1. *J Gen Virol* 69: 1531–1574
149. Medveczky MM, Geck P, Clarke C, Byrnes J, Sullivan JL, Medveczky PG (1989) Arrangement of repetitive sequences in the genome of herpesvirus sylvilagus. *J Virol* 63: 1010–1014
150. Meijer H, Dreesen JCFM, Van Boven CPA (1986) Molecular cloning and restriction endonuclease mapping of the rat cytomegalovirus genome. *J Gen Virol* 67: 1327–1342
151. Melendez LV, Daniel MD, Hunt RD, Garcis FG (1968) An apparently new herpesvirus from primary kidney cultures of the squirrel monkey (*Saimiri sciureus*). *Lab Anim Care* 18: 374–381
152. Melendez LV, Daniel MD, King NW, Calvo FC, Thorington RW, Jackman DA, Cadwallader J (1973) Isolation and in vitro characterization of a herpesvirus from field mouse (*Microtus pennsylvanicus*). *Lab Anim Sci* 23: 385–390
153. Melendez LV, Hunt RD, Daniel MD, Trum BF (1970) New World monkeys, herpesviruses, and cancer. In: H Balner, WIB Beveridge (eds) *Infectious and immunosuppression in subhuman primates*. Munksgaard, Copenhagen, pp 111–117
154. Melendez LV, Hunt RD, King NW, Barahona HH, Daniel MD, Fraser CEO, Garcia FG (1972) Herpesvirus ateles, a new lymphoma virus of monkeys. *Nature (New Biol)* 235: 182–184
155. Melendez LV, Hunt RD, King NW, Garcia FG, Like AA, Miki E (1967) A herpesvirus from sand rats (*Psammomys obesus*). *Lab Animal Care* 17: 302–309
156. Middelkamp JN, Patrizi G, Reed CA (1967) Light and electron microscopic studies of the guinea pig cytomegalovirus. *J Ultrastruct Res* 18: 85–101
157. Mirkovic R, Voss WR, Benyesh-Melnick M (1970) Characterization of a new herpes type virus indigenous for tree shrews. In: *Proceedings of the 10th International Congress of Microbiology, Mexico City*, pp 181–189
158. Monroe JH, Shibley GP, Schidlovsky G, Nakai T, Howatson AF, Wivel NW, O'Connor TE (1968) Action of snake venom on Rauscher virus. *J Natl Cancer Inst* 40: 135–145
159. Morgan C, Rose HM, Holden M, Jones EP (1959) Electron microscopic observations on the development of herpes simplex virus. *J Exp Med* 110: 643–656
160. Morgan C, Rose HM, Mednis B (1968) Electron microscopy of herpes simplex virus. I. Entry. *J Virol* 2: 507–516
161. Mosmann TR, Hudson JB (1973) Some properties of the genome of murine cytomegalovirus (MCV). *Virology* 54: 135–149
162. Nayak DP (1971) Isolation and characterization of a herpesvirus from leukemic guinea pigs. *J Virol* 8: 579–588
163. Nazerian K (1974) DNA configuration in the core of Marek's disease virus. *J Virol* 13: 1148–1150
164. Nesburn AB (1969) Isolation and characterization of a herpes-like virus from New Zealand albino rabbit kidney cultures: a probable re-isolation of virus III of Rivers. *J Virol* 3: 59–69
165. Nettleton PF, Sinclair JA, Herring JA, Inglis DM, Fletcher TJ, Ross HM, Bonniwell MA (1986) Prevalence of herpesvirus infectio in British red deer and investigations of further disease outbreaks. *Vet Rec* 118: 267–270
166. Neubauer RH, Rabin H, Strnad BC, Nonoyama M, Nelson-Rees WA (1979) Establishment of a lymphoblastoid cell line and isolation of a Epstein-Barr-related virus of gorilla origin. *J Virol* 31: 845–848
167. Nicholas J, Gompels UA, Craxton MA, Honess RW (1988) Conservation of sequence and function between the product of the 52-kilodalton immediate-early gene of herpesvirus saimiri and the BMLF1-encoded transcriptional effector (EB2) of Epstein-Barr virus. *J Virol* 62: 3250–3257
168. Nigida SM, Falk LA, Wolfe G, Deinhardt F (1979) Isolation of a cytomegalovirus from salivary glands of white-lipped marmosets (*Saguinus fuscicollis*). *Lab Anim Sci* 29: 53–60
169. Osterhaus ADME, Yang H, Spijkers HEM, Groen J, Teppema JS, Van Steenis G (1985) The isolation and partial characterization of a highly pathogenic herpesvirus from the harbor seal (*Phoca vitulina*). *Arch Virol* 86: 239–251.26
170. Parker JC, Vernon ML, Cross SS (1973) Classification of mouse thymic virus as a herpesvirus. *Infect Immun* 7: 305–308
171. Pellett PE, Biggin MD, Barrell B, Roizman B (1985) The Epstein-Barr virus may encode a protein showing significant amino acid and predicted secondary structure homology with the glycoprotein B of herpes simplex virus 1. *J Virol* 56: 807–813

172. Pensaert MB, Kluge JP (1989) Pseudorabies virus (Aujeszky's disease). In: Pensaert MB (ed) Virus infections of porcines. Elsevier, New York, pp 39–64
173. Plowright W, Ferris RD, Scott GR (1960) Blue wildebeest and the aetiological agent of bovine malignant catarrhal fever. *Nature* 188: 1167–1169
174. Plowright W, Macadam RF, Armstrong JA (1965) Growth and characterization of the virus of bovine malignant catarrhal fever in East Africa. *J Gen Microbiol* 39: 253–266
175. Plummer G, Goodheart CR, Henson D, Bowling CP (1969) A comparative study of the DNA density and behavior in tissue cultures of fourteen different herpesviruses. *Virology* 39: 134–137
176. Plummer G, Goodheart CR, Studdert MJ (1973) Equine herpesviruses: Antigenic relationships and DNA densities. *Infect Immun* 8: 621–627
177. Poffenberger KL, Roizman B (1985) Studies on non-inverting genome of a viable herpes simplex virus 1. Presence of head-to-tail linkages in packaged genomes and requirements for circularization after infection. *J Virol* 53: 589–595
178. Rafferty KA Jr (1965) The cultivation of inclusion-associated virus from Lucké tumour frogs. *Ann NY Acad Sci* 126: 3–21
179. Rajcani J, Blaskovic D, Svobodova J, Ciampor F, Huckova D, Stanekova D (1985) Pathogenesis of acute and persistent murine herpesvirus infection in mice. *Acta Virol* 29: 51–60
180. Randall CC, Ryden FW, Doll ER, Shell FS (1953) Cultivation of equine abortion virus in fetal horse tissue in vitro. *Am J Pathol* 29: 139–153
181. Rangan SRS, Martin LN, Bozelka BE, Wang N, Gormus BJ (1986) Epstein-Barr virus-related herpesvirus from a rhesus monkey (*Macaca mulatta*) with a malignant lymphoma. *Int J Cancer* 38: 425–432
182. Rasheed S, Rongey RW, Bruszewski J, Nelson-Rees WA, Rabin H, Neubaner RH, Esra G, Gardner MB (1977) Establishment of a cell line with associated Epstein-Barr like virus from a leukemic orangutan. *Science* 198: 407–409
183. Raynaud A, Adrian M (1970) Lésions cutanées à structure papillomateuse associés à des virus chez le lézard vert (*Lacerta virelis laur.*). *CR Acad Sci Ser D* 283: 845–847
184. Rebell G, Rywlin A, Haines H (1975) A herpesvirus-type agent associated with skin lesions of green sea turtle in aquaculture. *Am J Vet Res* 36: 1221–1224
185. Reid HW, Rowe LW (1973) The attenuation of a herpesvirus (malignant catarrhal fever virus) isolated from hartebeest (*Alcelaphus buselaphus cokei* Gunther). *Res Vet Sci* 15: 144–146
186. Roizman B (1990) An introduction to herpesviruses. In: Fields BN, Knipe DM et al (eds) *Fields' virology*, vol 2, 2nd edn. Raven Press, New York, pp 1787–1793
187. Roizman B, Carmichael LE, Deinhardt F, de The G, Nahmias AJ, Plowright W, Rapp F, Sheldrick P, Takahashi M, Wolf K (1981) Herpesviridae. Definition, provisional nomenclature and taxonomy. *Inter-virology* 16: 201–217
188. Roizman B, Furlong D (1974) The replication of herpesvirus. In: Fraenkel-Conrat H, Wagner RR (eds) *Comprehensive virology*, vol 3. Plenum, New York, pp 229–403
189. Roizman B, Sears AE (1990) Herpes simplex viruses and their replication. In: Fields BN, Knipe DM, et al (eds) *Fields' virology*, vol 2, 2nd edn. Raven Press, New York, pp 1795–1894
190. Rota PA, Maes RK, Ruyechan WT (1986) Physical characterization of the genome of feline herpesvirus 1. *Virology* 154: 168–179
191. Rowe WP, Capps WI (1961) A new mouse virus causing necrosis of the thymus in newborn mice. *J Exp Med* 113: 831–844
192. Sabin AB (1934) Studies of B virus. I: the immunological identity of a virus isolated from a human case of ascending myelitis associated with visceral necrosis. *Br J Exp Pathol* 15: 248–268
193. Sabin AB, Wright AM (1934) Acute ascending myelitis following a monkey bite with the isolation of a virus capable of producing the disease. *J Exp Med* 59: 115–136
194. Sabine M, Robertson GR, Whalley JM (1981) Differentiation of the subtypes of equine herpesvirus 1 by restriction endonuclease analysis. *Equine Vet J* 57: 148–149
195. Saito JK, Gribble DH, Berrios PE, Knight HD (1974) A new herpesvirus isolate from goats: preliminary report. *Am J Vet Res* 35: 847–848
196. Salahuddin SZ, Ablashi DV, Markham PD, Josephs SF, Sturzenegger S, Kaplan M, Halligan G, Biberfeld P, Wong-Staal F, Kramarsky B, Gallo RC (1986) Isolation of a new virus, HTLV, in patients with lymphoproliferative disorders. *Science* 234: 596–601
197. Schechter EM, Summers J, Ogston CW (1988) Characterization of herpesvirus isolated from woodchuck hepatocytes. *J Gen Virol* 69: 1591–1599

198. Schetter CH (1970) In vitro-Untersuchungen über die Eigenschaften des Virus der Hepatitis et Splenitis Infectiosa Strigum. In: Verhandlungsberichte des XII Internationalen Symposiums über Erkrankungen der Zootiere, Budapest, pp 205–209
199. Schneewis KE (1962) Serologische Untersuchungen zur Typendifferenzierung des herpesvirus hominis. *Z Immunitätsforsch Exp Ther* 124: 24–48
200. Schriemer EC, Wyatt LS, Yamanishi K, Rodriguez WJ, Frenkel N (1991) Differentiation between two distinct classes of viruses now classified as human herpesvirus 6. *Proc Natl Acad Sci USA* 88: 5922–5926
201. Schubert von G (1964) Elektronenmikroskopische Untersuchungen zur Pockenkrankheit des Karpfens. *Z Naturforsch* 19: 675–682
202. Shat KA, Calneck BW (1978) Characterization of an apparently nononcogenic Marek's disease virus. *J Natl Cancer Inst* 60: 1075–1082
203. Simpson CF, Hanley JE, Gaskin JM (1975) Psittacine herpesvirus infection resembling Pacheco's parrot disease. *J Infect Dis* 13: 390–396
204. Sixbey JW, Shirley P, Sloas M, Raab-Traub N, Israele V (1991) A transformation incompetent nuclear antigen 2-deleted Epstein-Barr virus associated with replicative infection. *J Infect Dis* 163: 1008–1015
205. Smith MG (1954) Propagation of salivary gland virus of the mouse in tissue cultures. *Proc Soc Exp Biol Med* 86: 435–440
206. Smith MG (1956) Propagation in tissue cultures of a cytopathogenic virus from human salivary gland virus (SGV) disease. *Proc Soc Exp Biol Med* 92: 424–430
207. Smith MG (1959) The salivary gland viruses of man and animals (cytomegalic inclusion disease). *Prog Med Virol* 2: 171–202
208. Spear PG, Roizman B (1972) Proteins specified by herpes simplex virus. V. Purification and structural proteins of the herpesvirion. *J Virol* 9: 431–439
209. Spring SB, Roizman B (1968) Herpes simplex virus products in productive and abortive infection. III. Differentiation of infectious virus derived from nucleus and cytoplasm with respect to stability and size. *J Virol* 2: 979–985
210. Stack MJ, Higgins RJ, Challones DJ, Gregory MW (1990) Herpesvirus in the liver of a hedgehog (*Erinaceus europaeus*). *Vet Rec* 620–621
211. Stannard LM, Fuller AO, Spear PG (1987) Herpes simplex virus glycoproteins associated with different morphological entities projecting from the virion envelope. *J Gen Virol* 68: 715–725
212. (deleted)
213. Stinski MF (1990) Cytomegalovirus and its replication. In: Fields BN, Knipe DM, et al (eds) *Fields' virology*, vol 2, 2nd edn. Raven Press, New York, pp 1959–1980
214. Storz H, Ludwig H, Rott R (1974) Immunologic and genetic relationship between herpes simplex virus and bovine herpes mammillitis virus. *Intervirology* 2: 1–13
215. Strandberg JD, Carmichael LE (1965) Electron microscopy of a canine herpesvirus. *J Bacteriol* 90: 1790–1791
216. Studdert MJ (1974) Comparative aspects of equine herpesviruses. *Cornell Vet* 64: 94–122
217. Studdert MJ, Simpson T, Roizman B (1981) Differentiation of respiratory and abortigenic isolates of equine herpesvirus 1 by restriction endonucleases. *Science* 214: 562–564
218. Sugaya K, Bradley G, Nonoyama M, Tanaka A (1990) Latent transcripts of Marek's disease virus are clustered in the short and long repeat regions. *J Virol* 64: 5773–5782
219. Sullivan DC, Atherton SS, Staczek J, O'Callaghan DJ (1984) Structure of the genome of equine herpesvirus type 3. *Virology* 132: 352–367
220. Thiry E, Bublot M, Dubuisson J, Pastoret PP (1989) Bovine herpesvirus-4 (BHV-4) infections of cattle. In: Witmann G (ed) *Herpesvirus diseases of cattle, horses, and pigs*. Kluwer, Norwell, pp 96–115
221. Thiry E, Dubuisson J, Bublot M, Van Bresseem M-F, Pastoret P-P (1990) The biology of bovine herpesvirus-4 infection of cattle. *DTW Dtsch Tierarzt Wochenschr* 97: 72–77
222. Todd WJ, Storz J (1983) Morphogenesis of a cytomegalovirus from an American bison affected with malignant catarrhal fever. *J Gen Virol* 64: 1025–1030
223. Trimble JJ, Desrosiers RC (1991) Transformation by herpesvirus saimiri. *Adv Cancer Res* 56: 335–355
224. Valicek L, Smid B, Pleva V, Mensik J (1970) Porcine cytomegalic inclusion disease virus. *Arch Ges Virusforsch* 32: 19–30
225. Wagner EK, Roizman B, Savage T, Spear PG, Mizell M, Durr FE, Sypowicz D (1970) Characterization of the DNA of herpesviruses associated with Lucke adenocarcinoma of the frog and Burkitt lymphoma of man. *Virology* 42: 257–261

226. Weller TH (1953) Serial propagation in vitro of agents producing inclusion bodies derived from varicella and herpes zoster. *Proc Soc Exp Biol Med* 83: 3440–3446
227. Whalley JM, Robertson GR, Davison AJ (1981) Analysis of the genome of equine herpesvirus type 1: arrangement of cleavage sites for restriction endonucleases *EcoRI*, *BglII* and *BamHI*. *J Gen Virol* 57: 307–323
228. Whalley JM, Webber CE (1979) Characteristics of Parma wallaby herpesvirus grown in marsupial cells. *J Gen Virol* 45: 423–430
229. Whalley JM, Robertson GR, Scott NA, Hudson GC, Bell CW, Woodworth LM (1986) Identification and nucleotide sequence of a gene in equine herpesvirus 1 analogous to the herpes simplex virus gene encoding the major envelope glycoprotein gB. *J Gen Virol* 70: 383–394
230. Whitley RJ (1990) Herpes simplex viruses. In: Fields BN, Knipe DM, et al (eds) *Fields' virology*, vol 2, 2nd edn. Raven Press, New York, pp 1843–1887
231. Wildy P, Watson DH (1963) Electron microscopic studies on the architecture of animal viruses. *Cold Spring Harbor Symp Quant Biol* 27: 25–47
232. Wolf K, Darlington RW (1971) Channel catfish virus: a new herpesvirus of ictalurid fish. *J Virol* 8: 525–533
233. Wolf K, Darlington RW, Taylor WG, Quimby MC, Nagabayashi T (1978) Herpesvirus salmonis: characteristics of a new pathogen of rainbow trout. *J Virol* 27: 659–666
234. Yamamoto T, Kelly RK, Nielson O (1983) Epidermal hyperplasias of Northern pike (*Esox lucius*) associated with herpesvirus and C-type particles. *Arch Virol* 79: 255–272
235. Zeigel RF, Clark HF (1972) Electron microscopic observation on a new herpes-type virus isolated from *Iguana iguana* and propagated in reptilian cells in vitro. *Infect Immun* 5: 570–582

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