Knowledge on the unique characteristics of parvoviruses containing only one strand of DNA has expanded rapidly during the last years. The single-stranded DNA molecule reveals a hairpin structure both at the 5’ and the 3’ end, and about 1% of the nucleic acid of the viruses belonging to the parvovirus genus forms double strands similar to the self-complementary strands of adenovirus species (AAV) and densovirus species [3, 26]. The suggestion that parvovirus particles contain a polymerase seems to be very unlikely in the light of new data [2]. Further experience regarding the polypeptides shows that mature virus particles have three polypeptides: VP-1 (mol.wt. 83,000), VP-2 (mol.wt. 65,000), and VP-3 (mol.wt. 60,000-62,000). All three polypeptides probably are derived from a common sequence during a late maturation step, as was shown for minute virus of mice (MVM) [31]. A number of other proteins ranging in size from 10,000 to 56,000 also are frequently detected in the gels. However, they seem to be nonessential for virus infection.

An important finding for rapid classification is the demonstration of a common FA polypeptide antigen in the genus Adeno-associated virus, which is shared by all AAVs [8]. Recent data suggest that the hepatitis A virus of man is not likely to be a parvovirus [21]. New candidate viruses which seem to have typical parvovirus properties, however, have been isolated and characterized. They include a parvovirus from rabbits [14], the Aleutian mink disease virus [23, 27] and an AAV from equines [7]. In addition, there are four new densovirus isolates from different Lepidoptera and Orthoptera species [11, 15-17]. References included in the report by Bachmann et al. [1] are not repeated in this review. For further information the reader is referred to the monograph by Siegl [28].
1.1 Family: Parvoviridae
Taxonomic status: Family with three genera: Parvovirus, Adeno-associated virus, and Densovirus.
Relationship with other groups: Unrelated to other families.
2 The virion
2.1 Chemical composition
2.1.1 Nucleic acid
DNA
Single-stranded
Linear
Number of pieces: Probably one.
Sedimentation coefficient: 15-18S (alkaline conditions).
Molecular weight: 1.5-2.2 × 10^6
Percentageweightofvinon: 19-32%.
Base composition (%):
Genus Parvovirus: G, 19.5-22.8; A, 22-26.8; C, 21.4-22.9; T, 29-33.4. GC value: 40.9-45.2.
Hairpin structure both at the 5' and the 3' end of the otherwise single-stranded molecule (about 99% unique single-strand encapsidated) [3].
Genus Adeno-associated virus: Minus strand: G, 26.3; A, 20.5; C, 26.3; T, 26.5. GC value: 53.0.
Plus strand: G, 26; C, 26.5; A, 25.2; T, 21.7. GC value: 53.1.
Nearest neighbor analysis: Results from three species within the genus Parvovirus are available and are very similar (table I). Homology studies: Hybridization experiments in vitro showed 60-70% homology among AAV types 1-4. Digestion of H-1, H-3 and Lu III Table I. Nearest neighbor analysis

<table>
<thead>
<tr>
<th>Sequence</th>
<th>MVM DNA</th>
<th>RV DNA</th>
<th>H-1 DNA</th>
</tr>
</thead>
<tbody>
<tr>
<td>ApA</td>
<td>123</td>
<td>91</td>
<td>94</td>
</tr>
<tr>
<td>CpA</td>
<td>75</td>
<td>78</td>
<td>72</td>
</tr>
<tr>
<td>GpA</td>
<td>67</td>
<td>34</td>
<td>69</td>
</tr>
<tr>
<td>CpT</td>
<td>67</td>
<td>69</td>
<td>75</td>
</tr>
<tr>
<td>GpT</td>
<td>47</td>
<td>75</td>
<td>53</td>
</tr>
<tr>
<td>GpC</td>
<td>51</td>
<td>38</td>
<td>59</td>
</tr>
<tr>
<td>TpA</td>
<td>62</td>
<td>61</td>
<td>55</td>
</tr>
<tr>
<td>GpG</td>
<td>59</td>
<td>57</td>
<td>49</td>
</tr>
<tr>
<td>CnG</td>
<td>15</td>
<td>20</td>
<td>18</td>
</tr>
<tr>
<td>GpC</td>
<td>48</td>
<td>49</td>
<td>54</td>
</tr>
</tbody>
</table>

RF DNA with restriction endonucleases suggests that between H-1 and H-3 there is 95% homology, between H-1 and Lu III only about 80% [25]. The two densonucleosis viruses (Gal-leria and Junonia) show 87% homology in their DNA [12].
Infectivity has been shown for AAV-1DNA.
Other features: AAV DNA and densovirus DNA contain single plus and minus self-complementary strands in separate virions which hybridize in vitro to form a double strand. About 1% of MVM particles contain minus strands which, upon extraction, re-anneal with complementary plus strand to give double-stranded DNA [3,14].
2.1.2 Proteins
Percentageweight of vitamin: 63-81%.
Number of polypeptides: Three. Usually three polypeptides can be demonstrated in mature parvovirus and AAV virions, which probably are all derived from a common sequence: VP-1, VP-2 and VP-3. VP-3, the smallest polypeptide, is derived from VP-2 during the maturation process [5,21,31,32]. With members of the genus Parvovirus, VP-2 can be converted in vitro to VP-3 with proteases. Densoviruses seem to have four structural poly-peptides [12,34].

2.1.2.3
Molecular weights of polypeptides: Genus Parvovirus

<table>
<thead>
<tr>
<th></th>
<th>VP-1</th>
<th>VP-2</th>
<th>VP-3</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rat virus</td>
<td>81,00</td>
<td>64,00</td>
<td>60,000</td>
</tr>
<tr>
<td>H-1</td>
<td>86,00</td>
<td>66,00</td>
<td>62,000</td>
</tr>
<tr>
<td>MVM</td>
<td>83,00</td>
<td>64,00</td>
<td>61,000</td>
</tr>
<tr>
<td>LulI</td>
<td>85,00</td>
<td>66,00</td>
<td>62,000</td>
</tr>
<tr>
<td>Bovine</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>parvovirus</td>
<td>86,00</td>
<td>77,00</td>
<td>67,000</td>
</tr>
</tbody>
</table>

Comparable data for all viruses. A variation of about 10% must be accounted for in the techniques used. All parvoviruses contain one major polypeptide (about 80% of the total protein). In RV, H-1, MVM, Lu III, and bovine parvovirus-1, VP-3 is the major polypeptide. Genus Adeno-assodated virus: AAV types 1-3 contain VP-1, 87,000; VP-2, 73,000; and VP-3, 62,000m. Genus Densovirus: VP-1, 98,000; VP-2, 72,000; VP-3, 57,000; and VP-4, 46,000 [13,34].

2.1.2.4
2.1.2.5
2.1.3
2.1.4
Number of protein subunits: 62-72 molecules per virion. Enzymes: Probably lacking. Lipids: None. Carbohydrates: None.
Since the major protein is found in the various species in different fractions, it should be indicated by addition of an ‘m’, e. g. VP-3m. Physicochemical properties

Density: Density of mature virions 1.39-1.42 g/cm³ in CsCl; particles with densities > 1.42 g/cm³ are probably ‘dense’ precursor particles; those banding between 1.34 and 1.38 g/cm³ most likely are defective particles [5, 19, 24, 28]. Empty particles have a density of 1.31 g/cm³. Sedimentation coefficient: 110-122S Weight in daltons: 5.5 × 10⁶ to 6.2 × 10⁶


Envelope: None. Cores
Site of accumulation of viral proteins 3 Nucleus.
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Nonstructural proteins: Two non-structural polypeptides (mol.wts. 24,900 and 15,800) were demonstrated during replication of AAV type 2 in KB cells [4].

Mode of nucleic acid replication

General account: Parental DNA is converted to linear duplex replicative forms (RF). One possible course is that RF DNA undergoes semiconservative replication at first. Following the burst of synthesis of viral proteins, the synthesis becomes asymmetric, favoring the production of single-stranded DNA and conserving the complementary strand in the RF. However, other modes of replication strategies are possible.

Effect of inhibitors: Any inhibitor of host cell DNA initiation or synthesis should inhibit parvovirus replication. Halogenated deoxyuridines, as well as cytosine arabinoside, actinomycin D, and α-amanitin, inhibit replication.

Site of maturation: Nucleus.

Other features:
Members of the genus Parvovirus require one or more cellular functions generated during the S or G2 phase of cell division, very probably during late S phase. One or more components of the cell DNA synthesizing apparatus probably required for the replication of viral DNA.
Members of the genus Adeno-assocciated virus require helper virus functions for measurable replication. Adenovirus coinfection leads to formation of new infectious virus. Co-infection with herpesviruses permits formation of immunofluorescent antigens and infectious DNA.

4 Cooperative interactions
Recombination: No data available.
Multiplicity reactivation: No data available.
Phenotypic mixing: There is some indication of phenotypic mixing between H-1, H-3 and Lu III viruses [28].

Other interactions: No data available.

5 Host range


Experimental

In vivo: In homologous or closely related hosts. Rodent viruses and Lu III agent also replicate in Syrian hamsters [30].

In vitro:

Genus Parvovirus: Cell cultures of homologous or closely related original host. Some rodent viruses also grow in cells of human origin. Adaptation to other cell cultures (hetero-logous) may be possible under certain conditions (e.g., PPV to human cell lines).

Genus Adeno-associated virus: With adenovirus as helper in a variety of different cell species.

Genus Densovirus: Cell cultures of homologous and related hosts. Cyto-pathic effects in L cells.

6 Pathogenicity

6.1 Association with diseases:


Genus Adeno-associated virus: None known.

Genus Densovirus: Densonucleoses 8.3 fatal for several insect species.

6.2 Tissue tropism:

9.1 Genus Parvovirus: All fast-replicating tissues, especially the vascular epithelium, the external germinal layer of the cerebellum, the intestinal epithelium, the odontoblastic tissues, 9.2 the hepatic parenchyma, the subependymal plate of the brain, fetal tissues, and tumors.

Genus Adeno-associated virus: All adenovirus-infected tissues.

Genus Densovirus: Multiply in most
of the tissues of larvae, nymphs and 9.3 adults.

6.3 Cytopathology: 9.4

Transmission
True vertical passage by ova is indicated for the goose parvovirus [6]. Transplacental transmissions have been detected for a number of species within the genus *Parvovirus*. The data on Lu III virus [30], Aleutian disease of mink [20] and the porcine parvo-viruses [10, 18] have been confirmed.

Horizontal: Yes. Vectors: Mechanically possible. Antigenic properties Number of distinct antigenic molecules in virion: The polypeptides of the virion are immunologically distinguishable; they are, however, antigenically related.
Antigens involved in virus neutralization: No data available. AAV and bovine parvovirus polypeptide sera do not show neutralization or react with whole virion using hemagglutination inhibition, complement fixation or immune electrophoresis. Number of distinct nonstructural antigens: No data available. Specificity of different antigens: Genus *Parvovirus*: Hemagglutinating, complement-fixing and neutralizing antigens are type-specific without cross-reaction, except for minor cross-reactions between RV, H-I and Paroviridae: Second Report

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MVM in the fluorescent antibody (FA) test.
All AAVs share a common antigen, as can be demonstrated by FA [8].

9.5 Antigenic properties used for classification: Demonstration of hemagglutinin, complement-fixing, immunofluorescing and neutralizing antigens.
10 Classification
Definition of family Paroviridae: Contain linear, single-stranded DNA. The molecular weight of the DNA is between 1.5 and 2.2 × 10^6. The virions are isometric, nonenveloped particles, 18-26 nm in diameter with icosahedral symmetry; probably 32 capsomers, 3-4 nm in diameter. Buoyant density in CsCl gradients is between 1.39 and 1.42 g/cm³ for the infectious particle. The viruses are ether- and chloroform-resistant, heat- and acid-stable (56°, pH 3 for 60min). The virion contains a hemagglutinin in many types, which has different activities for a variety of red blood cells. The virus multiplies in the nucleus, and the replication is dependent upon certain functions of the host cell or helper functions provided by other viruses.

Definition of genera:
Genus *Parvovirus*: Viruses replicate without a helper in susceptible cell cultures, mature virus particles only contain plus strands of DNA. Type species: Parvovirus r-1 (rat virus).
Other species belonging to genus *Parvovirus*:
Rat virus
H-1 virus
Minute virus of mice
Porcine parvovirus
Bovine parvovirus
Feline parvovirus [9]
Goose parvovirus
TVX
Lul][
RT[11] Possible members:
Gastroenteritis virus of man (Nor-
walk and Norwalk-like agents)
Aleutian mink disease virus (differing polypeptide pattern) [23]
Lapine parvovirus [14]
Canine parvovirus Genus Adeno-associated virus: Replication dependent upon helper viruses
(adenoviruses) for complete virion production, but infectious AAV, DNA and
immunofluorescent antigens are made in the presence of herpesviruses. Mature virus particles
contain either plus or minus strands of DNA that are complementary and come together in vitro
to form a double strand. All AAVs share a common antigen demonstrable by fluorescent
antibody techniques. Type species: AAV type 1 Other species belonging to genus Adeno-
associated virus:
AAV type 1
AAV type 2
AAV type 3
AAV type 4
Bovine AAV (X7)
Canine AAV [33]
Avian AAV (AAAV) Possible member:
rus; however, the single strands of the DNA are either plus or minus, are complementary, and
come together in vitro to form double strands. Type species: Densovirus of Galleria. Other
species belonging to genus Densovirus:
Densovirus of Galleria Densovirus of junonia Possible members: Densovirus of Aedes
Diatraea [17]
Acknowledgments
For preparation of the data sheet, the files of the WHO Collaborating Centre for Collection and
Evaluation of Data on Comparative Virology, Munich, FRG, were consulted.
References
(1975).