Human Parvoviruses

- **Family : Parvoviridae**
- **Small viruses (in Latin, parvum meaning small)**
- **genome: ssDNA**
- **One known human pathogen (parvovirus B19)**
- **Parvoviridae consists of two subfamilies:**
  - **Densovirinae ……. contains viruses of insects**
  - **Parvovirinae……..contains viruses of vertebrates**

Family *Parvoviridae*

parvus (Latin) = small

Hosts: mammals
birds
insects

Disease: erythema infectiosum (B19 virus)

Used as: gene vectors (dependoviruses)

Virion

- Icosahedral
- 18–26 nm diameter
- Genome: single-stranded DNA
  4–6 kb
  linear





John Wiley & Sons, 2007

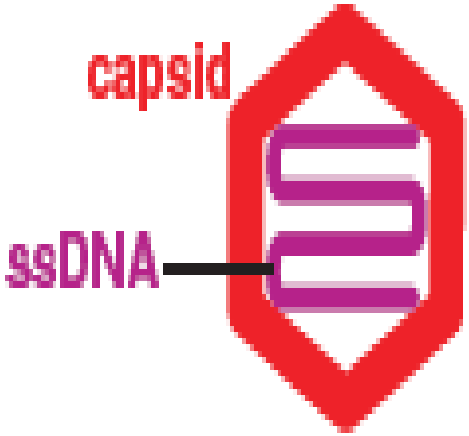
Some of the viruses in the family *Parvoviridae*

Subfamily	Genus	Species
Parvovirinae	*Dependovirus*	Adeno-associated virus 2
	Parvovirus	Minute virus of mice
		Feline panleukopenia virus
	Erythrovirus	B19 virus
	Bocavirus	Human bocavirus
Densovirinae	*Iteravirus*	*Bombyx mori* densovirus

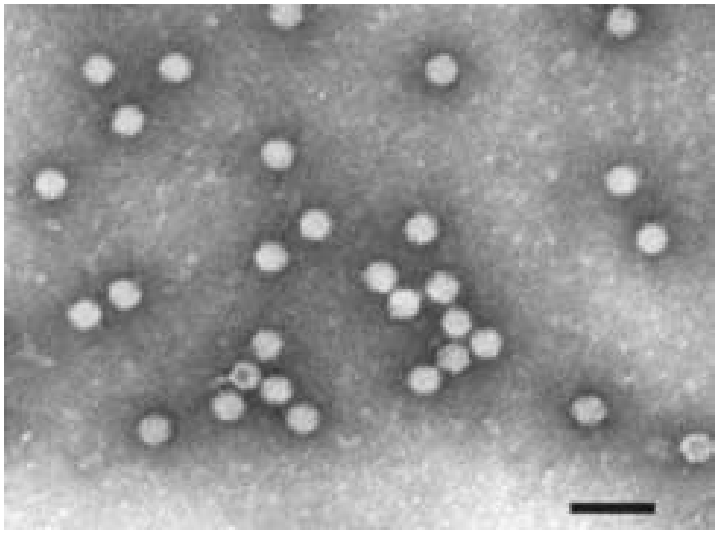
Subfamily parvovirinae

Subfamily	Genus	Virus	Host
Parvovirinae	*Parvovirus*	Canine parvovirus—CPV	Dogs, foxes
		Mice minute virus—MVM	Mice
		Porcine parvovirus—PPV	Pigs
		Feline parvovirus—FPV	Cats
	Dependovirus	Adeno-associated virus 1–6—AAV	Humans, primate
		Avian adeno-associated virus—AAAV	Birds
		Canine adeno-associated virus—CAAV	Dogs
		Bovine adeno-associated virus—BAAV	Cattle
	Erythrovirus	Parvovirus B19—B19V	Humans
		Simian parvovirus—SPV	Primates
		Rhesus parvovirus—RhPV	
		Pigtailed macaque parvovirus—PtPV	
	Bocavirus	Bovine bocavirus	Cows
		Canine bocavirus	Dogs
		Human bocavirus—HBoV	Humans
	Amdovirus	Aleution mink disease virus	Minks
	Unclassified	Parv4	Humans

Parvovirus virion



A) Virion components



B) Electron micrograph of negatively stained virions

Walters *et al.,2004, Journal of Virology,* 78, 3361

Genus Parvovirus

- **Contains a wide range of viruses of mammals and birds**
- **First isolated as contaminants of cell cultures**
- **Have unknown primary hosts**
- **No member of this family is known to infect humans**

(Gao et al., 2002)

Parvovirus B19

- **Discovered initially in serum of an asymptomatic blood donor as a cause of false positive results in dx of HBsAg**

(Cossart et al.,1975)

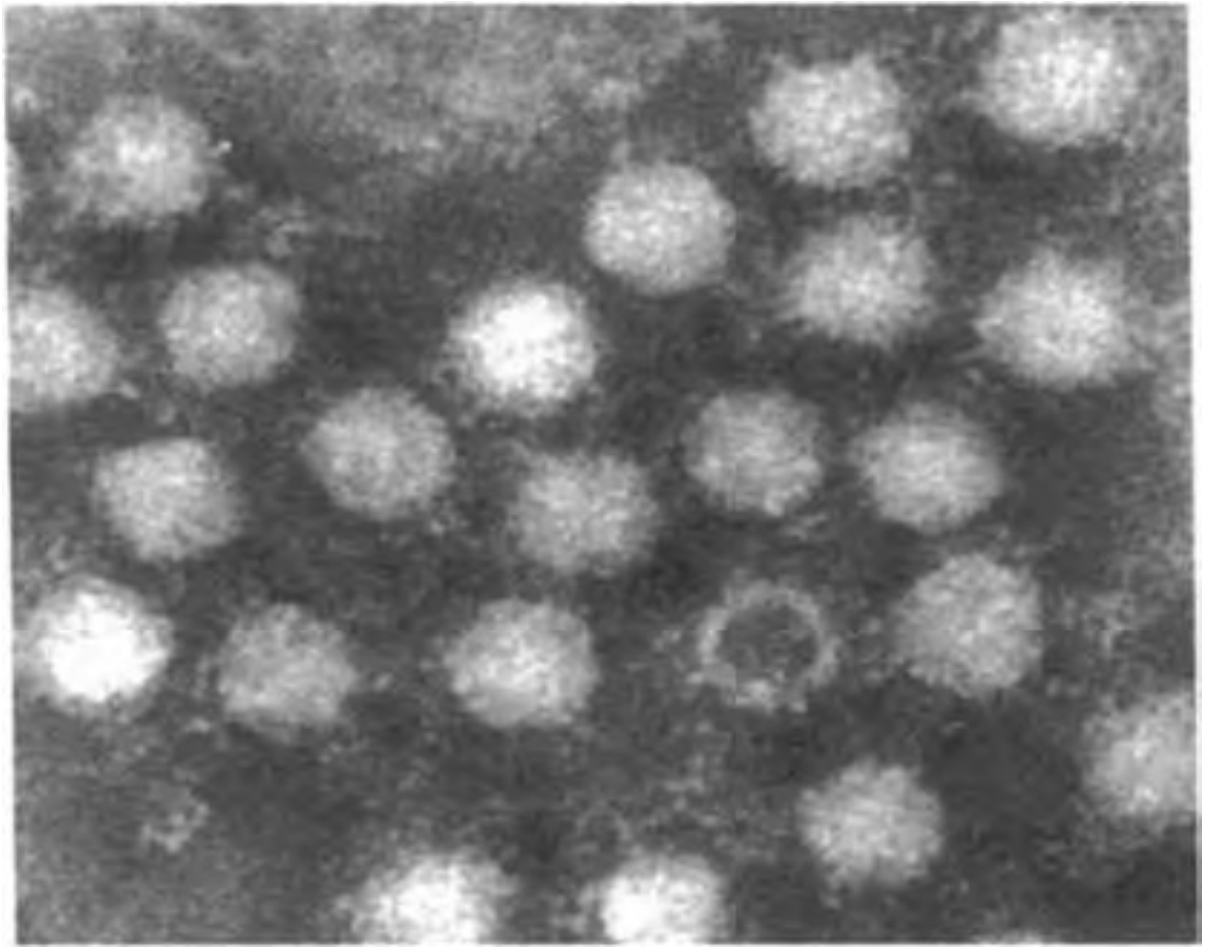
- **In 1983 the chemical nature of the agent was described**

(Summers et al., 1983)

Structure

- In electron micrographs of negatively stained preparations B19V appears as :
  - Non-enveloped
  - Icoashedral with a diameter varying from 18 to 25 nm
- The virus do not contain lipids or carbohydrates
- As with all parvovirus particles, B19V:
  - Stable over a wide range of pH
  - Resistant to lipid solvents
  - Not quite resistant to heat as other parvoviruses
  - Inactivated by formalin, oxidizing agents & γ-irradiation

(Blumel et al., 2002)



Appearance of B19V particles by electron microscopy

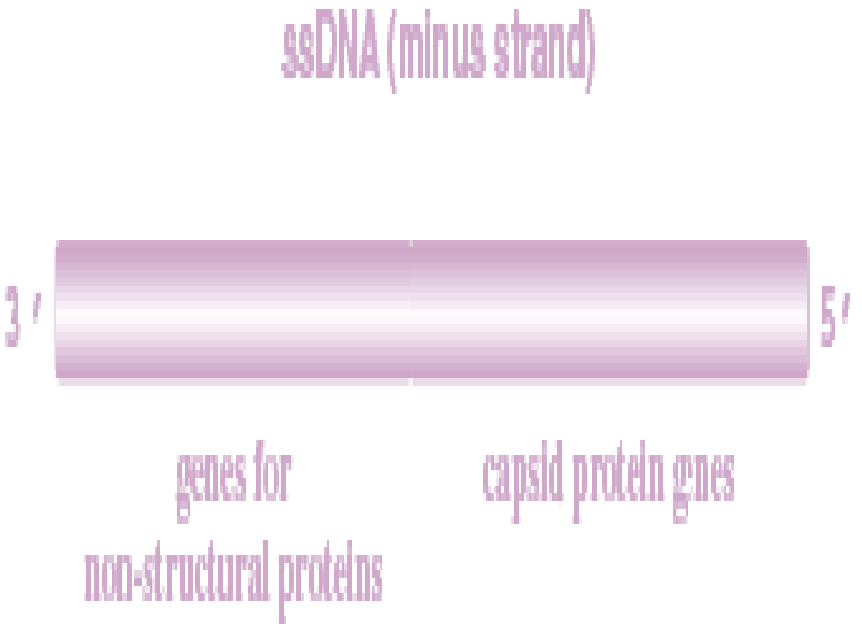
Genome Organization

- **Parvovirus B19 encapsidates both positive & negative ssDNA with equal frequency**

- **The genome of B19V is one of the largest among the**

Parvoviruses comprising 5596 nucleotides & with long (365 nucleotides)

In a (−) DNA the genes for non-structural proteins are towards 3’ end & the structural protein genes are towards the 5’ end



Parvovirus genome organization

Non structural (NS) protein:

- **Has DNA-binding properties**
- **Has adenosine and guanosine triphosphatase activity**
- **Possesses nuclear localization signals**
- **Essential for B19V infectivity and DNA replication**

(Zhi *et al., 2006)*

- **Expression of the NS protein causes host cell death through triggering caspases & induction of apoptosis**

- **Two structural proteins in B19V:**

  ►VP1(84 kDa) and VP2 (58 kDa)

- **VP2 is the major capsid protein, with only ~5% VP1 in the infectious particle**

- **The major cellular receptor for B19, globoside or P antigen binds to VP2**

Parvovirus replication

- **Parvovirus can encode only a few proteins, so the virus**

depends on its host cell (or another virus) to provide

important proteins

- **Some of these cell proteins:**

- **a DNA polymerase &**

- **Other proteins involved in DNA replication are available only during the initial phase of the cycle when DNA synthesis occurs**

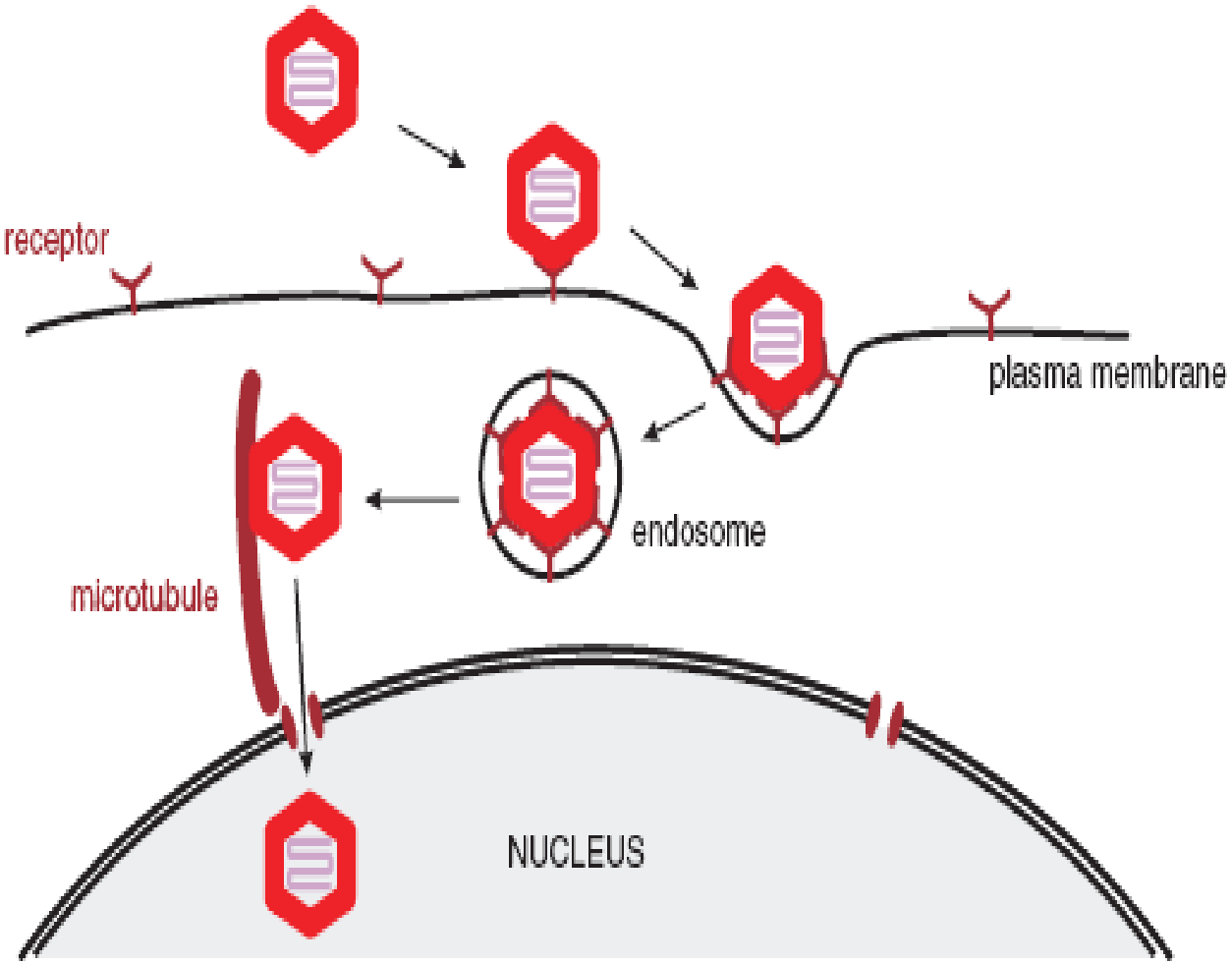
- **A virion attaches to receptors on the surface of a host cell**

- **In the case of B19 virus, the host cell is a red blood cell precursor & the receptor is the blood group P antigen**

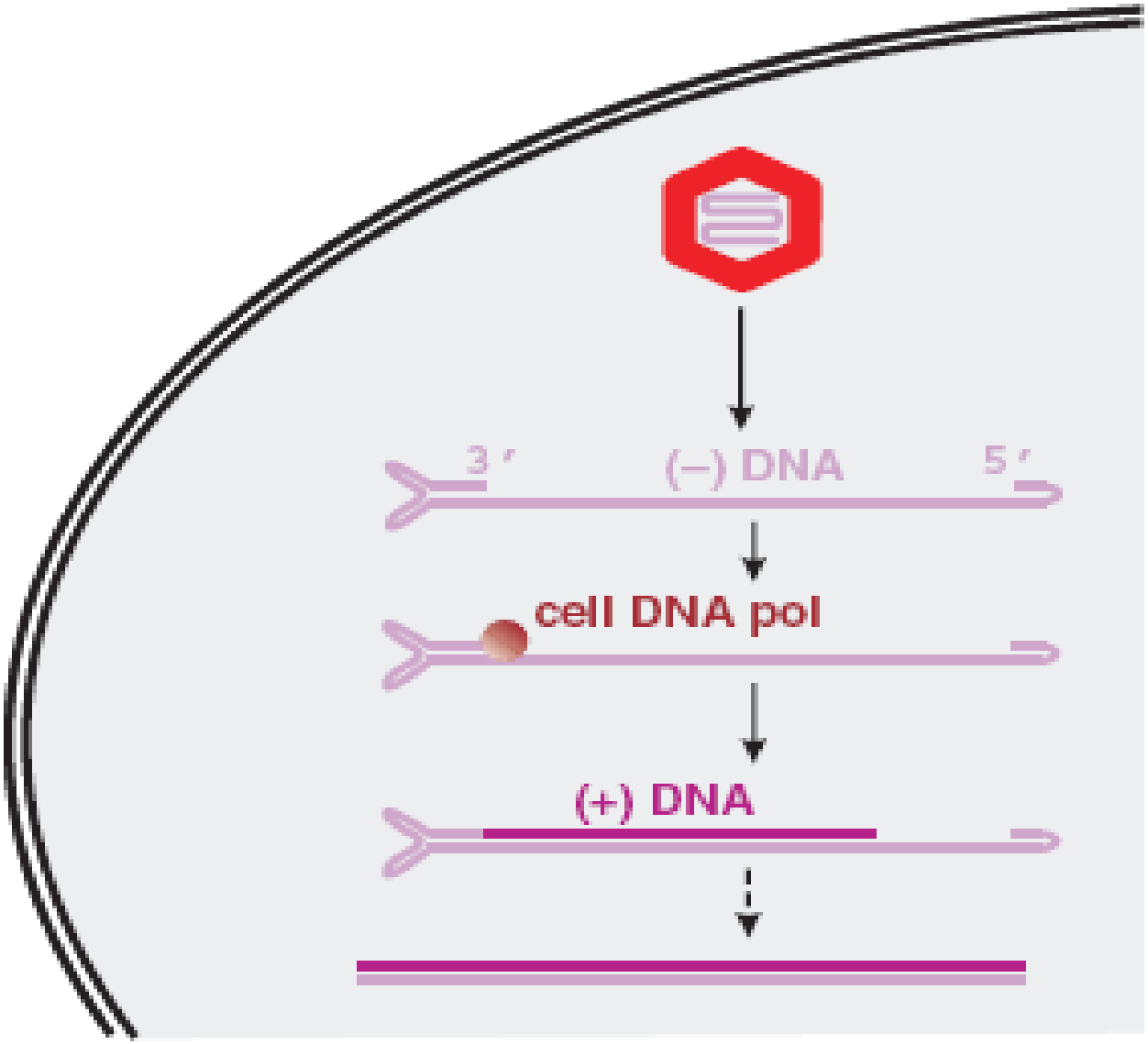
- **The virion enters the cell by endocytosis & is released from the endosome into the cytoplasm**

  ► **Associates with microtubules & transported to a nuclear pore**

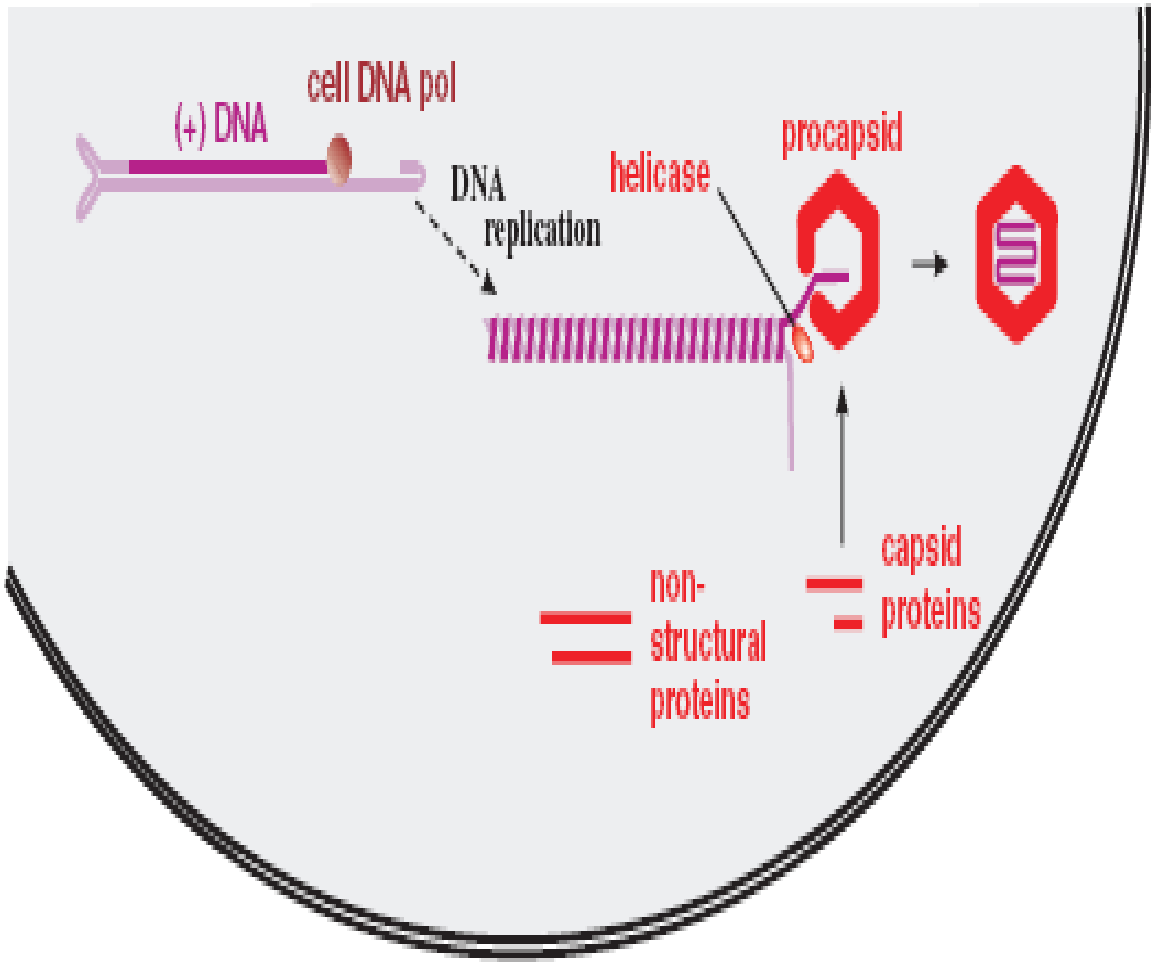
N.B: **virion must undergo some structural changes before it can be transported into the nucleus**



Parvovirus attachment and entry



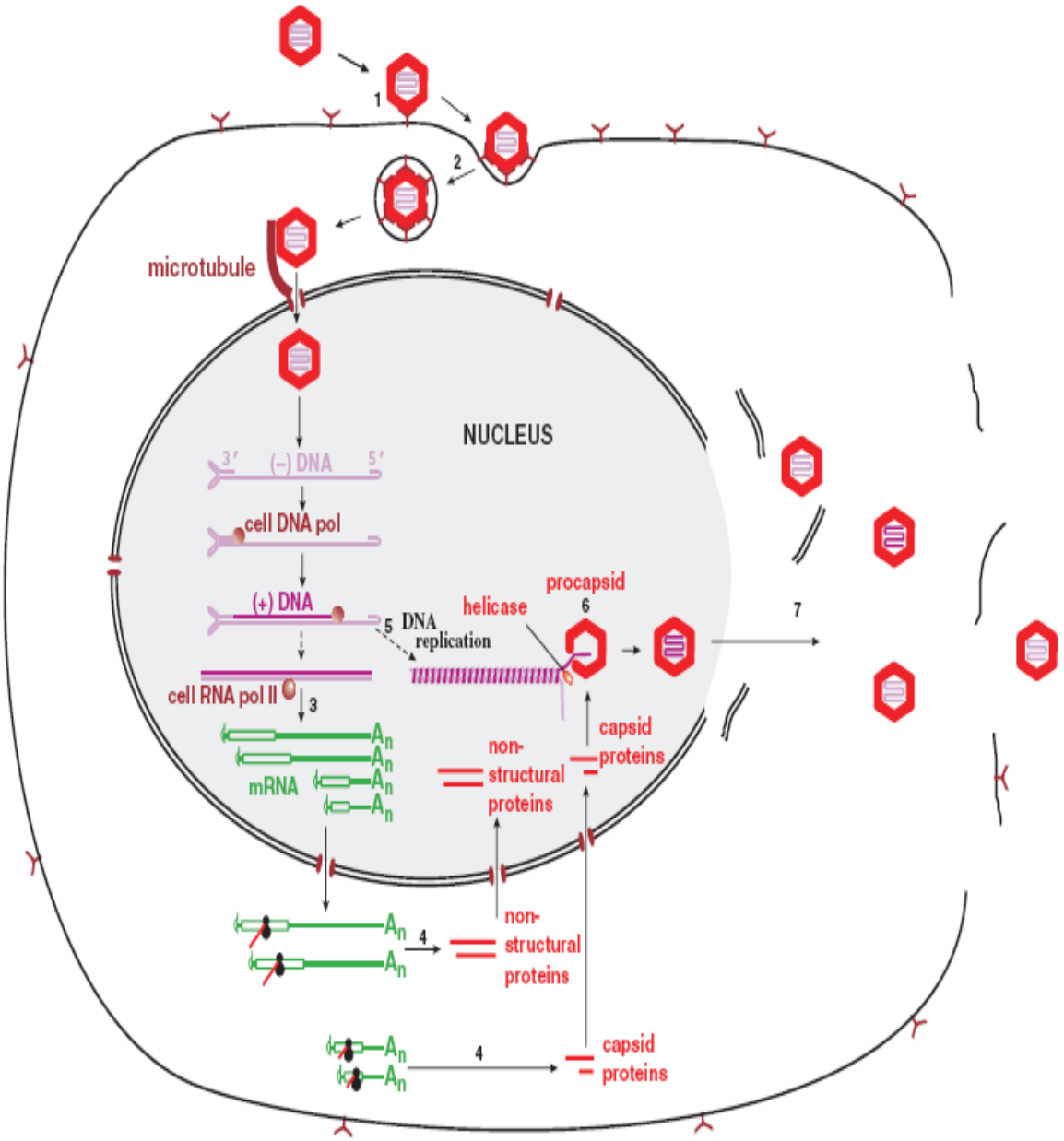
ssDNA converted to dsDNA by cell DNA polymerase



Parvovirus virion assembly

Parvovirus replication cycle

1. Attachment
2. Entry
3. Transcription
4. Translation
5. Assembly
6. Genomic repln
7. Excite



Pathogenesis

Studies have showed wo phases:

1. First phase of the illness

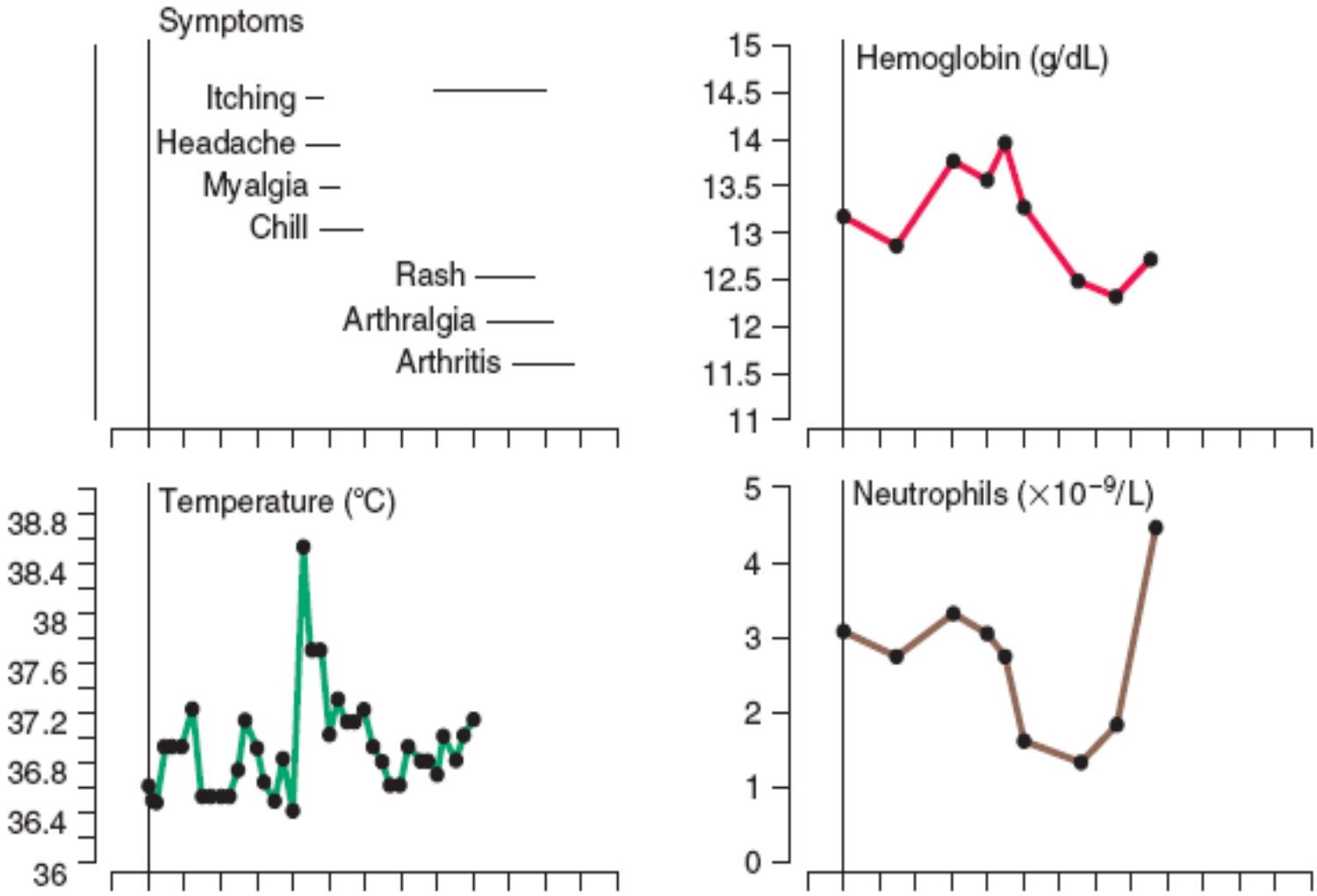
Characterized by viremia that develops in about 6 days
after intranasal inoculation of B19 into susceptible host

- **Viremia lasts about 1 week (IgM developed)**
- **IgG antibodies develop several days later and persist indefinitely**

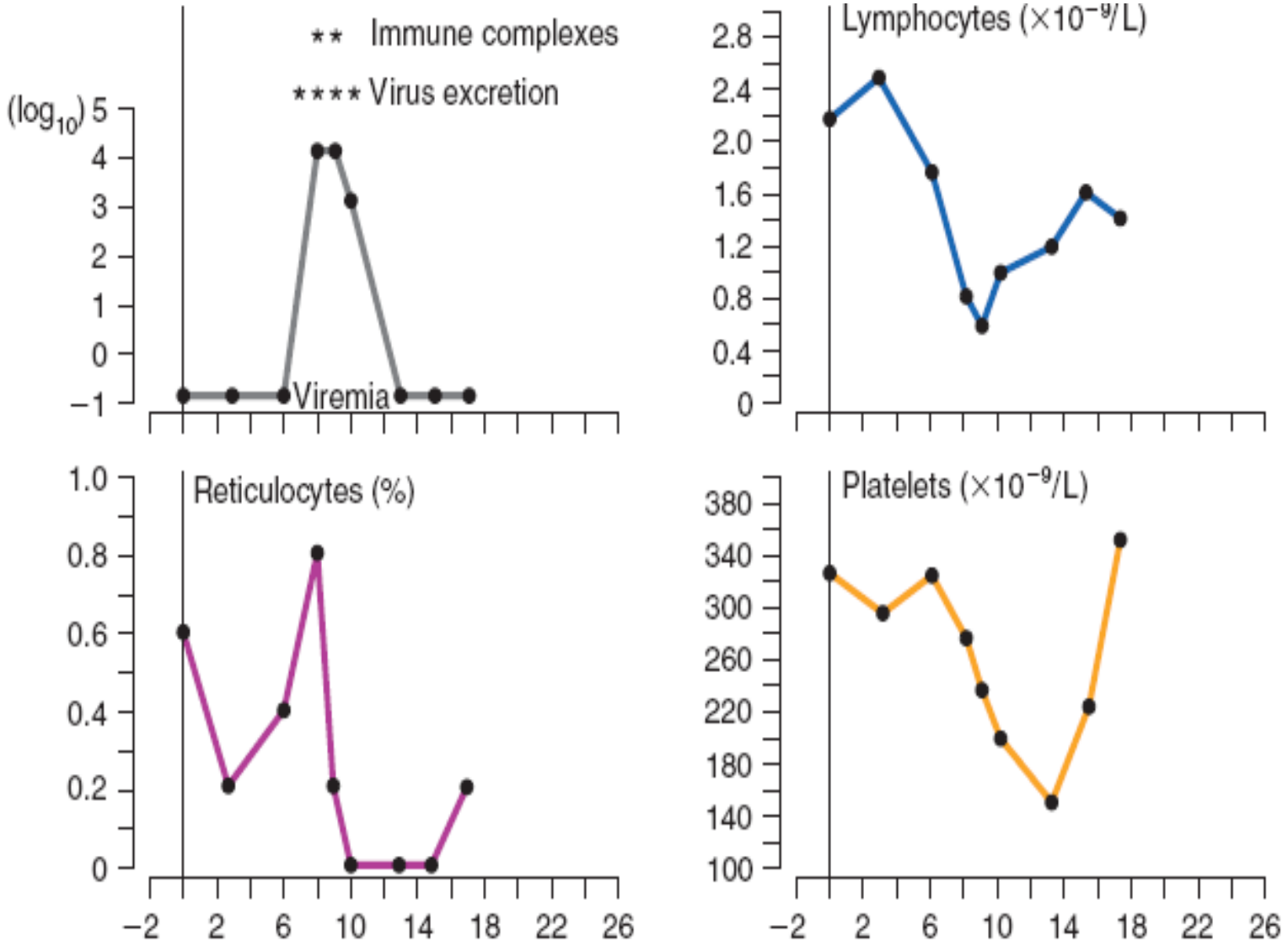
- **Non-specific systemic symptoms lasting 2 or 3 days occur early during the viremic phase, include:**
  - **Headache, malaise, myalgia, fever, chills, and pruritus**
  - **Accompanied by reticulocytopenia & excretion of virus from respiratory tract**
- **Several days after the onset of symptoms:**
  - **Decline in hemoglobin conc. (maintained for 7 to 10 days)**
  - **Examination of bone marrow samples reveals a marked depletion of erythroid precursor cells**
  - **Transient mild lymphopenia, neutropenia, & throbocytopenia**

2. A second phase

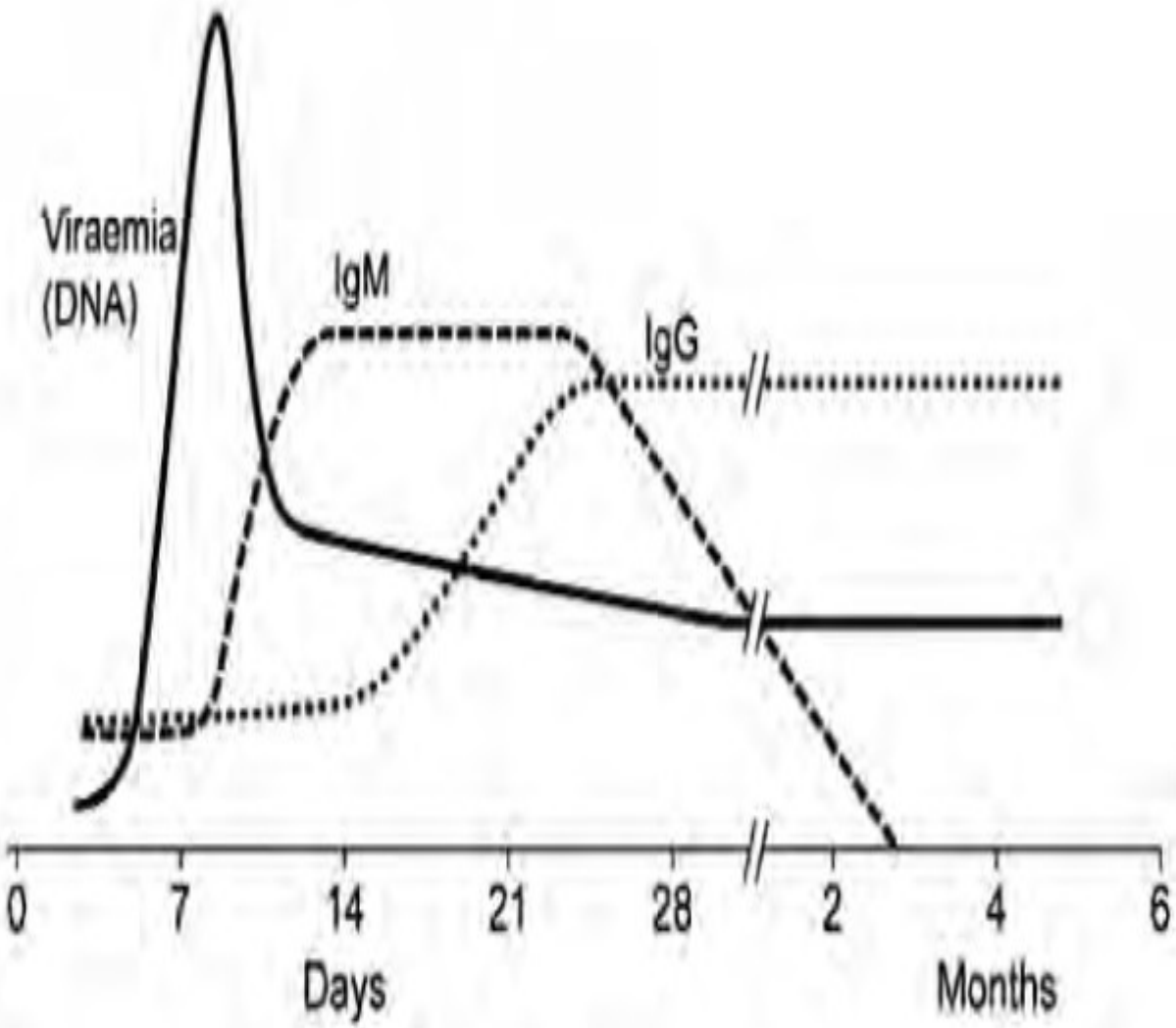
- **Begins around 17 or 18 days after virus inoculation & after:**
  - **Clearance of viremia**
  - **Cessation of viral shedding in throat secretions**
  - **Resolution of reticulocytopenia**
- **This phase occurs in the presence of rising serum titters of antibody to B19**



Features of primary parvovirus infection (Harison , 16th edition)


** Immune complexes
**** Virus excretion
(log10) 5
4
3
2
1
0
−1
Viremia
Lymphocytes (×10−9/L)
2.8
2.4
2.0
1.6
1.2
0.8
0.4
0
Reticulocytes (%)
1.0
0.8
0.6
0.4
0.2
0
Platelets (×10−9/L)
380
340
300
260
220
180
140
100
−2
2
6
10
14
18
22
26
Days after inoculation

B19 Serology



Epidemiology of parvovirus B19

- **orldwide**
- **Affect all age group**
- **Infection occurs throughout the year in temperate climates**
- **Outbreaks are more common in late winter**

Transmission

- **Clearly unknown but, may be respiratory or through direct contact**
- **B19 can be transmitted during therapy with clotting factor**
- **Is now known that infusion of plasma pools containing high titre virus (>10^7 IU ml^{-1}) can transmit infection**

B19V Infection in Pregnancy

- **Maternal B19 infections usually do not adversely affect the fetus**
- **It is estimated that fewer than 10% of maternal B19 infections in the first 20 weeks of pregnancy lead to fetal death**

Laboratory diagnosis

Specimens:

- **Serum (principal specimen)**
- **Tissue biopsy**

A. Virus Detection

Culture of B 19 in erythroid progenitor cells derived from:

- **Human bone marrow, umbilical cord, peripheral blood,or fetal liver sources**

- **Failed to grow in conventional cell culture lines & animal model**

B. Serologic tests

- **ELISA (detection of B19-specific IgM & IgG Abs)**
- **Haemagglutination-based assays**

C. Molecular technique

- **Detection of viral DNA by quantitative PCR is the mainstay of detection of B19V**

- **Low levels of viral DNA (<10^4 IU (genome copies) ml^{-1}) can**

be detected for months, or even years after acute infection

Treatment

- **No specific treatment / vaccine for B19V infection**

Prevention and control

- **Isolating of infected individuals**
- **Vaccination of animals to prevent animal B19V**