PARVOVIRUS B19

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Parvovirus B19

1- Taxonomy

2- Bocavirus

- Detected in some respiratory tract infections & may GI infections, but not proved to cause infections as they were associated with other viruses when isolated
- Infect children mainly

3- Structure and general properties

Virion: Icosahedral, 18–26 nm in diameter, 32 capsomeres

Composition: DNA (20%), protein (80%)

Genome: Single-stranded DNA, linear, 5.6 kb, MW 1.5–2.0 million

Proteins: One major (VP2) and one minor (VP1)

Envelope: None

Replication: Nucleus, dependent on functions of dividing host cells

Outstanding characteristics:
Very simple viruses
Human pathogen, B19, has tropism for red blood cell progenitors
One genus contains viruses that are replication-defective and require a helper virus

4- Pathogenesis, replication & Clinical Manifestations

Syndrome	Host or Condition	Clinical Features
Erythema infectiosum	Children (fifth disease) Adults	Cutaneous rash Arthralgia-arthritis
Transient aplastic crisis	Underlying hemolysis	Severe acute anemia
Pure red cell aplasia	Immunodeficiencies	Chronic anemia
Hydrops fetalis	Fetus	Fatal anemia

1) The virus enter the body to the blood until it reaches the bone marrow
2) infects erythroid progenitor cells because they're mitotic active and have p antigens
3) kill infected cells and spread in blood causing viremia
4) After about 4 days of infection, the DNA of the virus can be detected in the blood, and the reticulocytes and platelets will start to decrease
5) After about 8-10 days in average, some general symptoms will appear 6) Immune response by B cells will start after viremia, IgM antibodies will start to rise after about 8 days and IgG antibodies will start rising after about 12 days, they will end the viremia by forming immune complexes, the general symptoms will disappear and number of platelets and reticulocytes will return normal
7) Immune complexes will deposit in some organs causing Erythema Infectiosum, such as the cheeks of the face causing skin rash (Fifth Disease), and the joints of the body (usually both hands, wrists, knees and feet) causing arthralgia and arthritis

5- Epidemiology

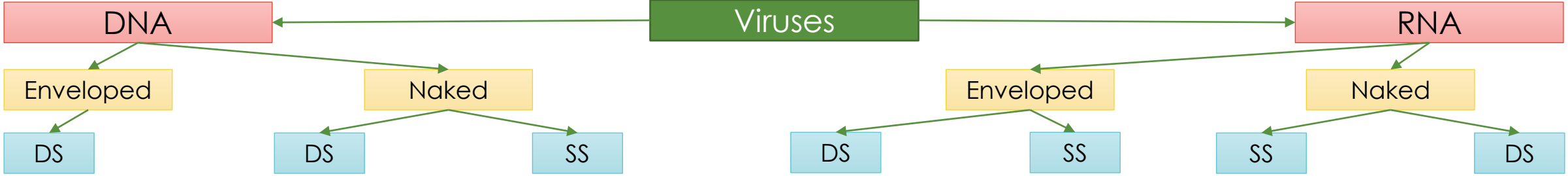
- Susceptibility to cause infections = 20% - 50%
- Not known to cause seasonal epidemics

6- Diagnosis

- parvo: PCR or serological assays
- boca: only PCR

7- Treatment & prevention

- Treatment is usually supportive
- There is no vaccine and anti-viral treatment for parvovirus b19 & bocavirus
- We sometimes passively immunize immunocompromised patients



Parvoviridae (Ic)

Parvovirus B19

Bocaviruses

Guidelines:
SS: single stranded
DS: Double stranded
Ic: Ichosahedral capsid
He: Helical capsid
Co: Complex capsid

Parvoviridae

Parvovirinae

Densovirinae

Erythrovirus Bocavirus Dependovirus Amdovirus Protoparvovirus

Genotype 1 (B19) Genotype 2 Genotype 3

1.5% to 11.3%

Children

Acute weezing

With other virus infections

PCR

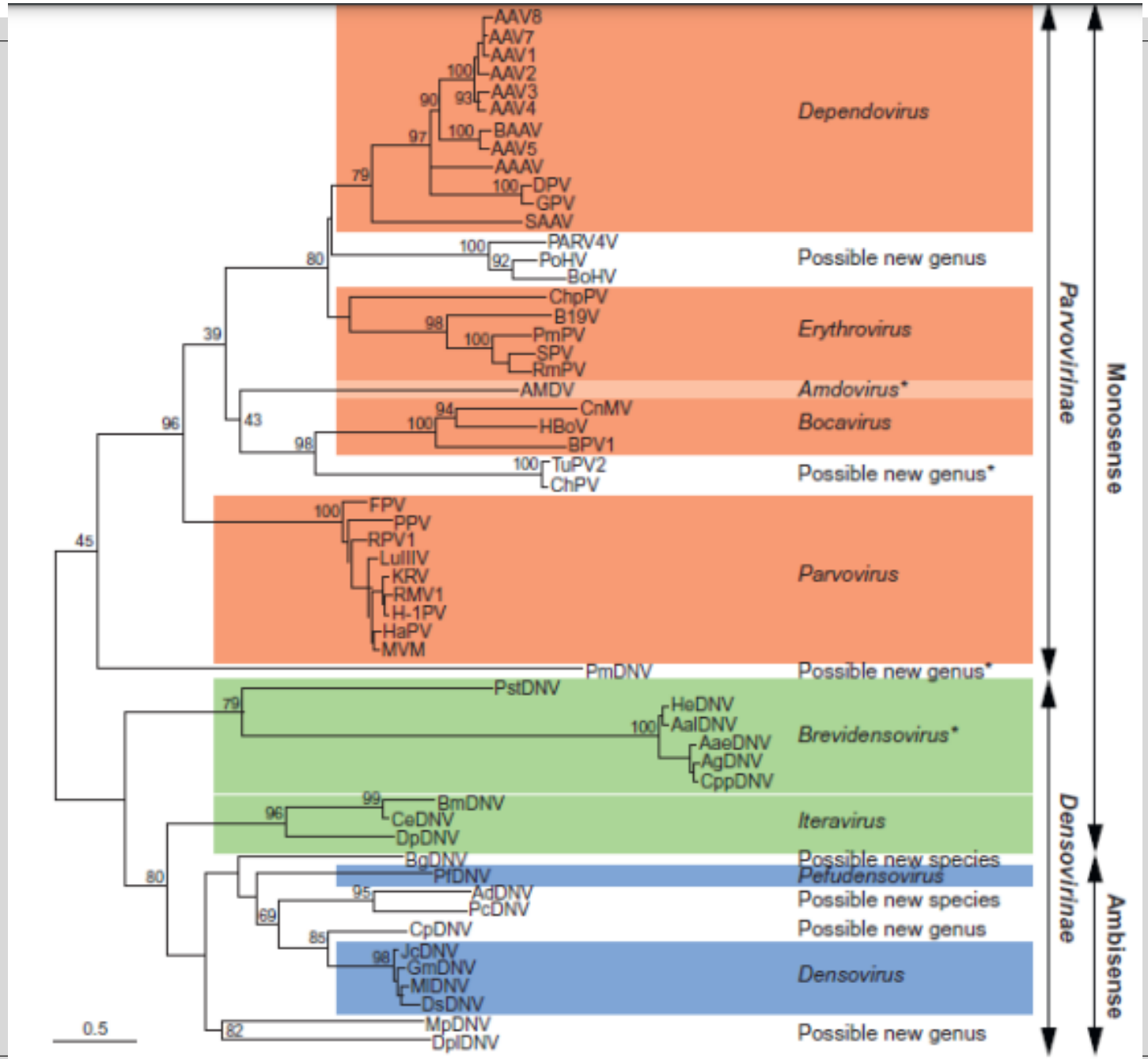
No treatment

3% of stool samples

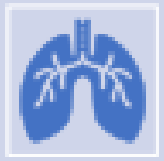
With other virus infections

Co-infection

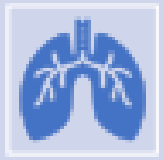
Mechanism is unknown


AAV8
AAV7
AAV1
AAV2
AAV3
AAV4
BAAV
AAV5
AAAV
DPV
GPV
SAAV
Dependovirus
PARV4V
PoHV
BoHV
Possible new genus
ChpPV
B19V
PmPV
SPV
RmPV
Erythrovirus
AMDV
Amdovirus*
CnMV
HBoV
BPV1
Bocavirus
TuPV2
ChPV
Possible new genus*
FPV
PPV
RPV1
LuIIIV
KRV
RMV1
H-1PV
HaPV
MVM
Parvovirus
PmDNV
Possible new genus*
PstDNV
HeDNV
AalDNV
AaeDNV
AgDNV
CppDNV
Brevidensovirus*
BmDNV
CeDNV
DpDNV
Iteravirus
BgDNV
Possible new species
PfDNV
Pefudensovirus
AdDNV
PcDNV
Possible new species
CpDNV
Possible new genus
JcDNV
GmDNV
MlDNV
DsDNV
Densovirus
MpDNV
DplDNV
Possible new genus
0.5
Parvovirinae
Densovirinae
Monosense
Ambisense

Human Bocavirus Infections



Human bocavirus has been detected in 1.5% to 11.3% of respiratory tract samples from young children with respiratory infections.



It is prevalent among children with acute wheezing. However, bocavirus is often found in mixed infections with other viruses, so it remains unclear if bocavirus is the cause of acute respiratory disease in children.

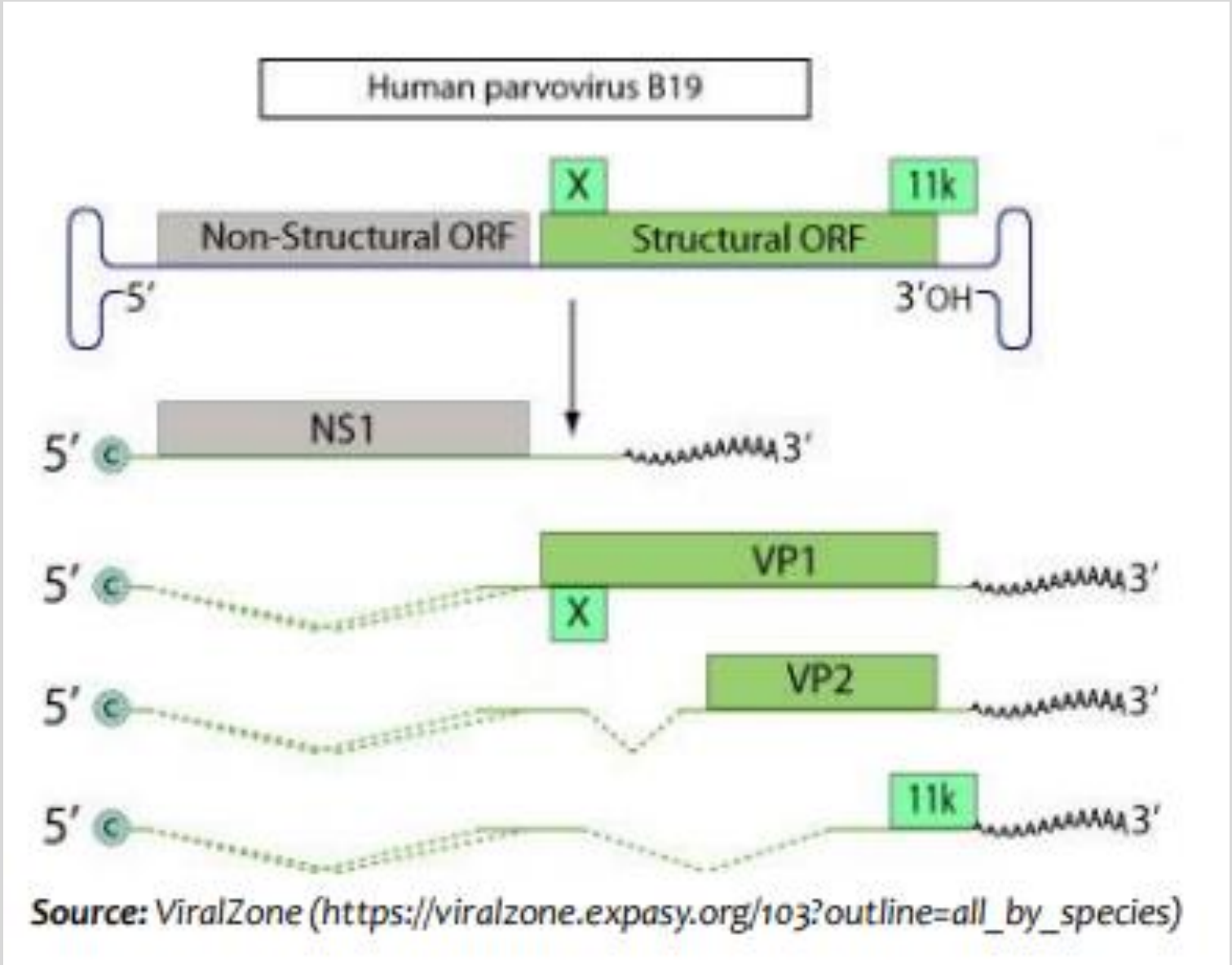
The virus has been detected in about 3% of stool samples from children with acute gastroenteritis. Coinfection rates with other enteric pathogens were high, so any causative role of bocavirus in gastroenteritis is unknown.

3- Structure & general properties

- Genome: Single stranded linear DNA, about 5kb, it composes about 20% of the total virus
- Envelope: No envelope
- Capsid: Icosahedral capsid, it's diameter is 18-26 nm, and is composed of many subunits that can be divided into two types: vp2 (the major capsid protein) & vp1 (the major capsid protein), the capsid composes about 80% of the whole virus

3- Structure & general properties

- Simplest and smallest DNA virus
- Replicates in nucleus & depends on functions of dividing host cells
- Extremely resistant to inactivation, they're stable between a pH of 3 and 9 and withstand heating at 56°C for 60 minutes, but they can be inactivated by formalin, β-propiolactone, and oxidizing agents
- There is one genotype that is considered a defective virus from the parvovirus b19 (need a helper virus)
  - Autonomous parvoviruses have 5k+ genomes compared to 4k+ genome in defective parvoviruses; also, the autonomous viruses encapsulate DNA strands complementary to viral mRNA, while defective parvoviruses have DNA of both polarities



Source: *ViralZone (https://viralzone.expasy.org/103?outline=all_by_species)*

3- Structure & general properties

- 1.Structural proteins: Virions contain two coat proteins that are encoded by an overlapping, in-frame DNA sequence:
  VP1: The minor structural protein, It is bigger in size because additional amino acids on N terminus. The N terminus of VP1 is located on the external part of virion capsid and contains many neutralizing epitopes which are linear in nature.
  VP2: The major capsid protein, VP2, represents about 90% of virion protein. VP2 is identical in sequence to the carboxy portion of VP1, and it is smaller than VP1. VP2 epitopes are conformational in nature.
- 2.Non structural proteins: (NS1) : Proteins that causes apoptosis in infected cells.

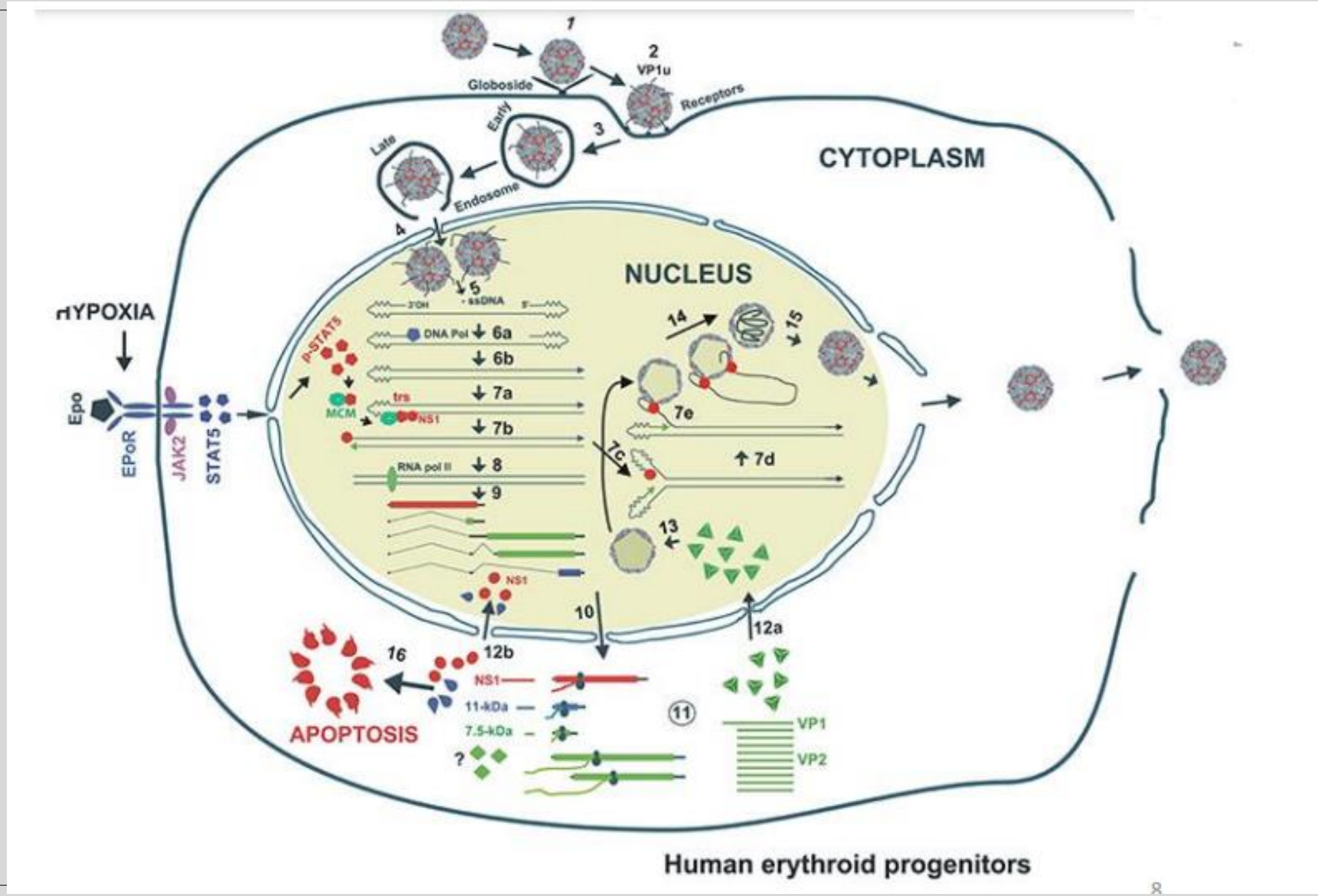
4- Pathogenesis, replication & Clinical Manifestations

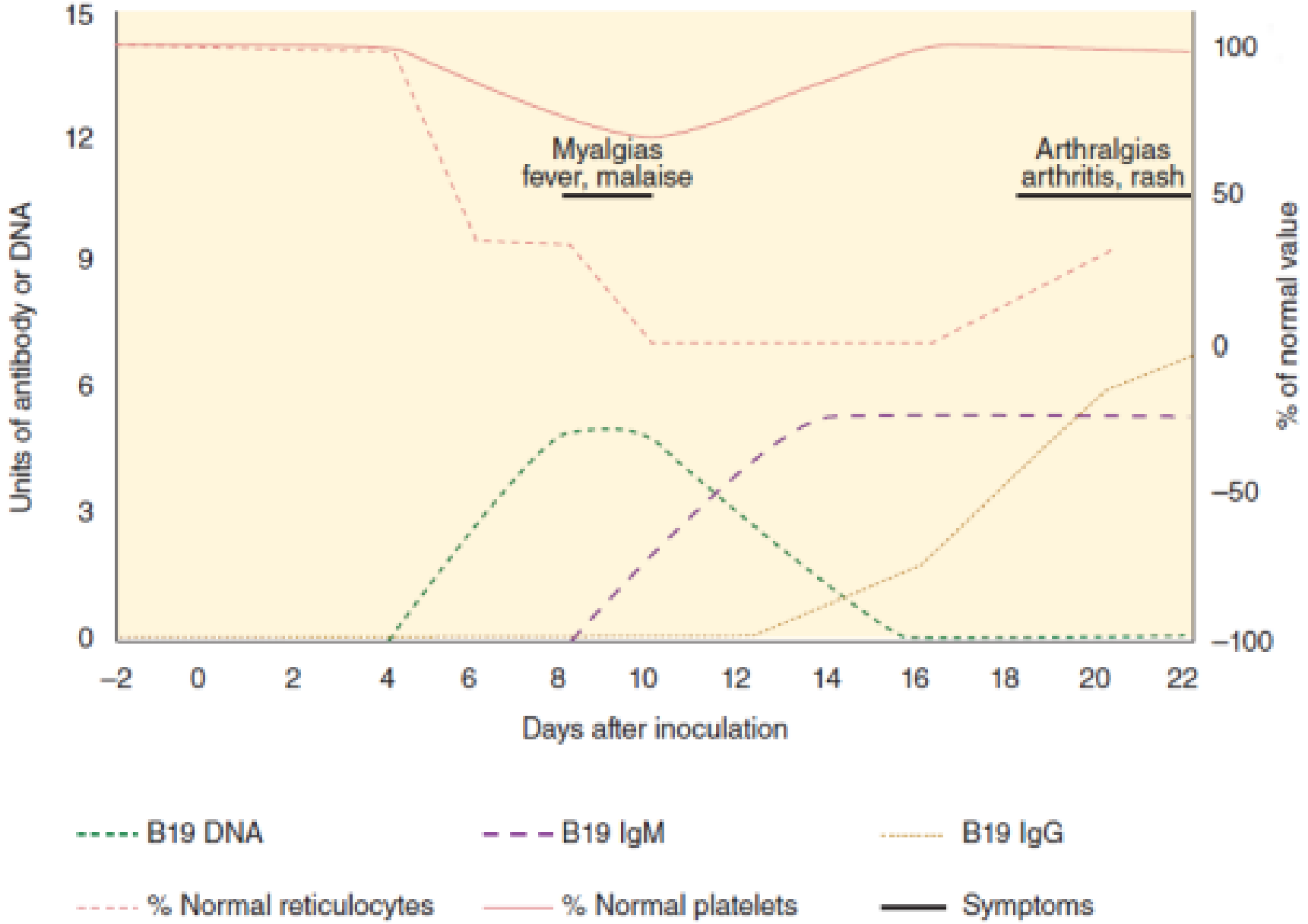
- 1) The virus enter the body through the respiratory system mainly, it moves to the blood until it reaches the bone marrow
  2) In the bone marrow, it infects erythroid progenitor cells or proerythroblast , it infects them because of three reasons:
  a- They have "p antigen" on their surface that is important for the penetration of the virus (receptor mediated endocytosis)
  b- they are mitotic active, and this is important for the replication of the virus
  c- They have co-receptors "b1a5" that helps in the penetration of the viruses
  Note: they may infect also megakaryocyte cells (precursor of platelets)
  3) They start to replicate in the infected cells, producing structural proteins for the new capsids, and non-structural proteins (NP1) that will lead to apoptosis of the infected cells, so they will spread in the blood causing viremia

4- Pathogenesis, replication & Clinical Manifestations

- 4) After about 4 days of infection, the DNA of the virus can be detected in the blood, and the reticulocytes and platelets will start to decrease
- 5) After about 8-10 days in average, some general symptoms will appear like myalgia, malaise and fever will appear
- 6) Immune response by B cells will start after viremia, IgM antibodies will start to rise after about 8 days and IgG antibodies will start rising after about 12 days, they will end the viremia by forming immune complexes, the general symptoms will disappear and number of platelets and reticulocytes will return normal
- 7) Immune complexes will deposit in some organs causing Erythema Infectiosum, such as the cheeks of the face causing skin rash (Fifth Disease), and the joints of the body (usually both hands, wrists, knees and feet) causing arthralgia (joints pain) and arthritis (joints inflammation)

Note: Fifth Disease usually appears in children, while arthralgia and arthritis usually appear in adults (not always)

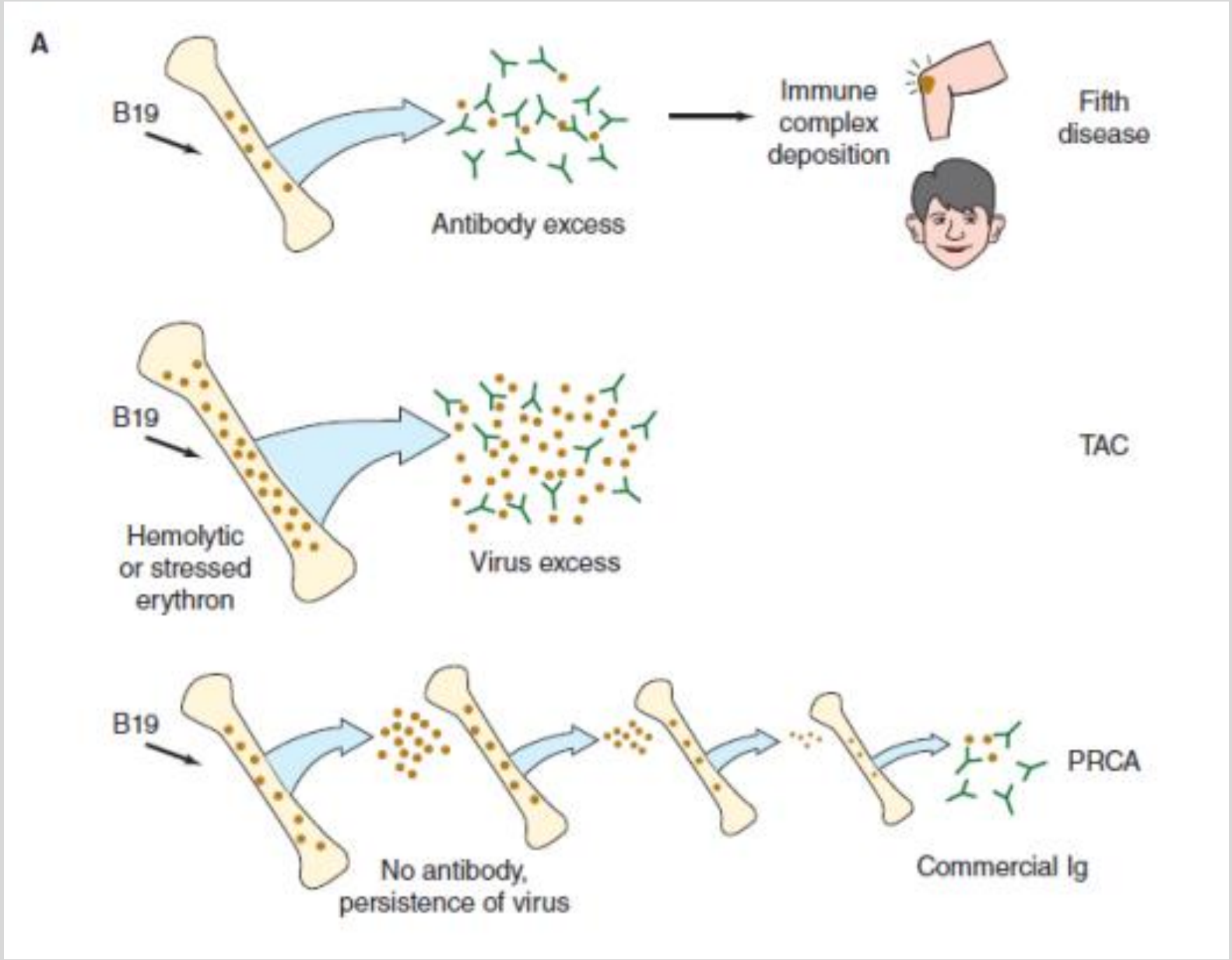

1
2
VP1u
Globoside
Receptors
Early
3
Late
Endosome
CYTOPLASM
4
5
NUCLEUS
HYPOXIA
Epo
EPoR
JAK2
STAT5
p-STAT5
3'OH
+ ssDNA
5'
DNA Pol
6a
6b
7a
7b
trs
MCM
NS1
RNA pol II
8
9
14
15
7e
7c
7d
13
NS1
10
12a
12b
16
APOPTOSIS
NS1
11-kDa
7.5-kDa
?
11
VP1
VP2
Human erythroid progenitors

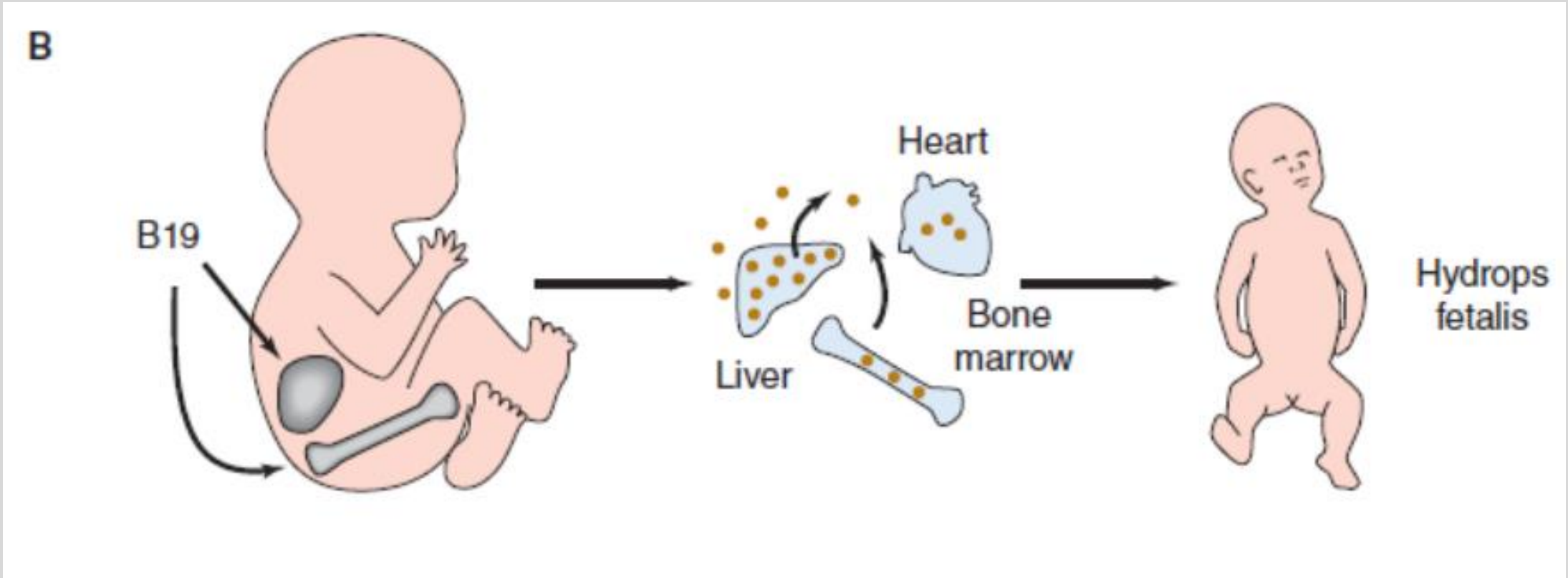

15
12
9
6
3
0
Units of antibody or DNA
100
50
0
−50
−100
% of normal value
Myalgias
fever, malaise
Arthralgias
arthritis, rash
−2
0
2
4
6
8
10
12
14
16
18
20
22
Days after inoculation
B19 DNA
B19 IgM
B19 IgG
% Normal reticulocytes
% Normal platelets
Symptoms

4- Pathogenesis, replication & Clinical Manifestations

- In normal individuals, the disease is self limited and the only manifestations are general symptoms and **erythema infectiosum**
- If the patient is immuno-compromised (e.g AIDS infected), he will suffer from a persistent infections with subsequent chronic suppression of BM resulting in chronic anemia, we call this manifestation **Pure red cell aplasia**
- If the patient have low amounts of red blood cells such as the fetus and people suffering from chronic hemolytic anemia diseases previously, they will have severe manifestations
  1- people suffering from chronic hemolytic anemia diseases (such as in patients with sickle cell disease, thalassemias, and acquired hemolytic anemias in adults) : they will suffer from an abrupt cessation of RBC synthesis in the BM and is reflected in the absence of erythroid precursors in the BM, accompanied by a rapid worsening of anemia, this case is called **Transient Aplastic Crisis**
  2- The heart will beat rapidly to condense the function of the lost blood, causing blood plasma to leak outside the capillaries, leading to **Hydrops fetalis** which is fatal

Syndrome	Host or Condition	Clinical Features
Erythema infectiosum	Children (fifth disease)	Cutaneous rash
	Adults	Arthralgia-arthritis
Transient aplastic crisis	Underlying hemolysis	Severe acute anemia
Pure red cell aplasia	Immunodeficiencies	Chronic anemia
Hydrops fetalis	Fetus	Fatal anemia


A
B19
Antibody excess
Immune complex deposition
Fifth disease
B19
Hemolytic or stressed erythron
Virus excess
TAC
B19
No antibody, persistence of virus
Commercial Ig
PRCA


B
B19
Heart
Liver
Bone
marrow
Hydrops
fetalis

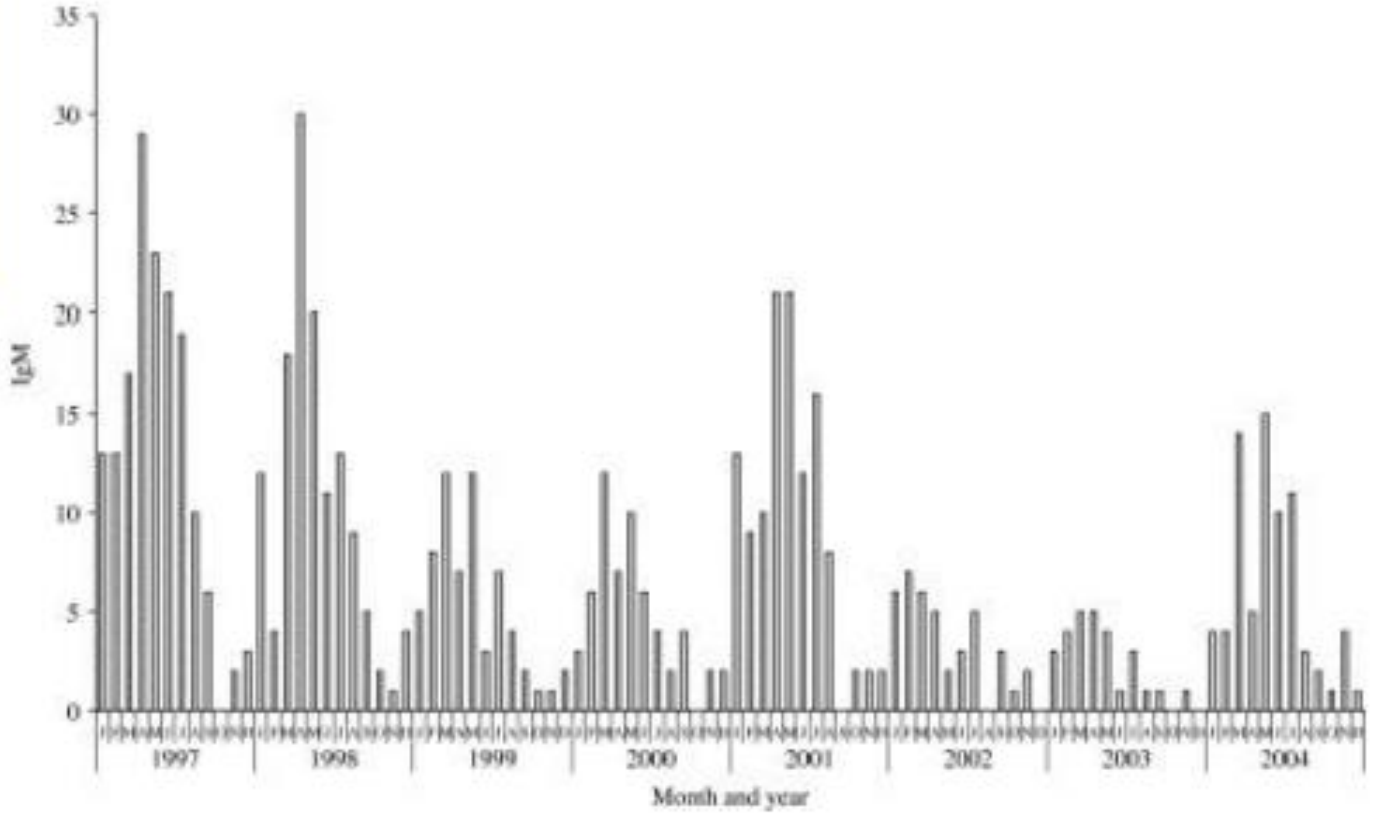
5- Diagnosis

- PCR (the most sensitive), probe hybridization of serum or tissue extracts, and in situ hybridization of fixed tissue.
- Serologic assays; Antigen detection assays; Immunohistochemistry.
- Virus isolation is not used to detect infection.
- The only assay currently available for human bocavirus is PCR.

Parvoviruses – Epidemiology

Estimates of attack rates in susceptible contacts range from 20% to 50%

→ There is no seasonal epidemics for the parvovirus B19



7- Treatment

- Treatment is usually supportive for the symptoms only
- There is no vaccine and anti-viral treatment for the parvovirus b19 and the bocavirus
- We sometimes passively immunize immunocompromised patients by giving them intravenous antibodies against parvovirus b19 if they are infected