4- Parvoviruses

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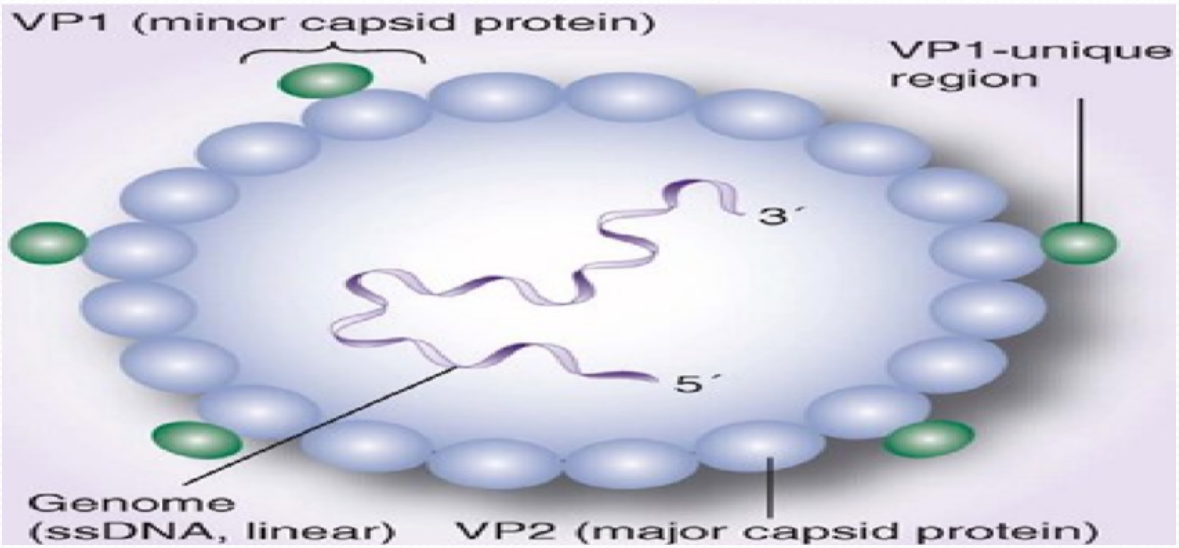
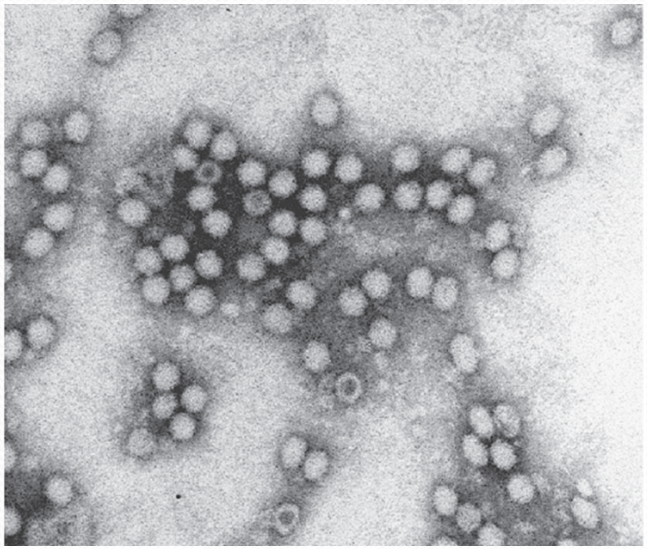
Objectives

- Describe general structure, properties, replication and control of Parvovirus
- Describe the virology, epidemiology, pathogenesis, clinical presentation and management of Parvovirus B19

Structure

- Parvoviruses are very small (18 to 26 nm), naked virions that contain a linear single-stranded DNA (the smallest DNA animal viruses)
- Icosahedral with 32 capsomers and 2 protein coats (VP2 and VP1)
- Parvovirus B19 is pathogenic for humans





Replication and control

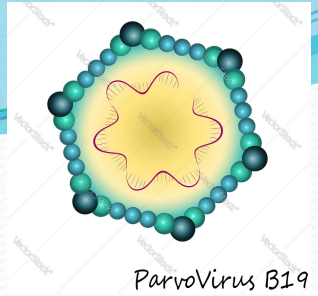
- Because of the limited coding capacity of their genome, viral replication is dependent on functions supplied by replicating host cells or by coinfecting helper viruses
- Autonomously replicating and defective parvoviruses that require a helper virus for replication.
- It is difficult to culture human B19 parvovirus
- Viral DNA replication occurs in the nucleus
- Viral replication results in cell death
- Virions are extremely resistant to inactivation.
  - They are stable between a pH of 3 and 9
  - Withstand heating at 56°C for 60 minutes
  - Can be inactivated by formalin, and oxidizing agents

TABLE 31-1 Important Properties of Parvoviruses

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:
Environmentally stable
Human pathogen, B19, has tropism for red blood cell progenitors.

Parvovirus B19 Infections

Viral target

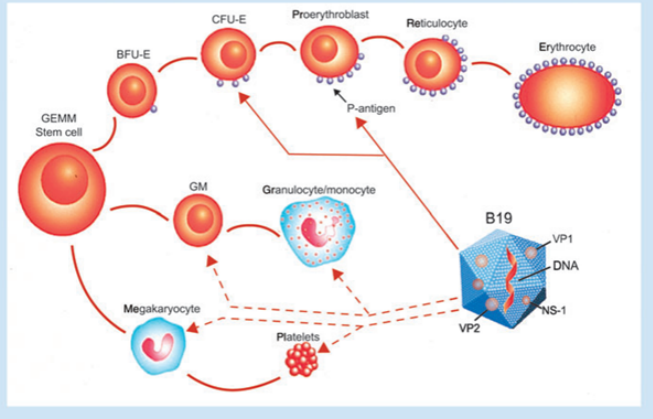


- The cellular receptor for B19 is blood group P antigen (globoside).
- P antigen is expressed on mature erythrocytes, erythroid progenitors, megakaryocytes, endothelial cells, placenta, and fetal liver and heart, which helps explain the narrow tissue tropism of B19 virus
- the major sites of virus replication in patients are assumed to be the adult marrow, some blood cells, and the fetal liver
- A primary site of replication appears to be the nucleus of an immature cell in the erythrocyte lineage.

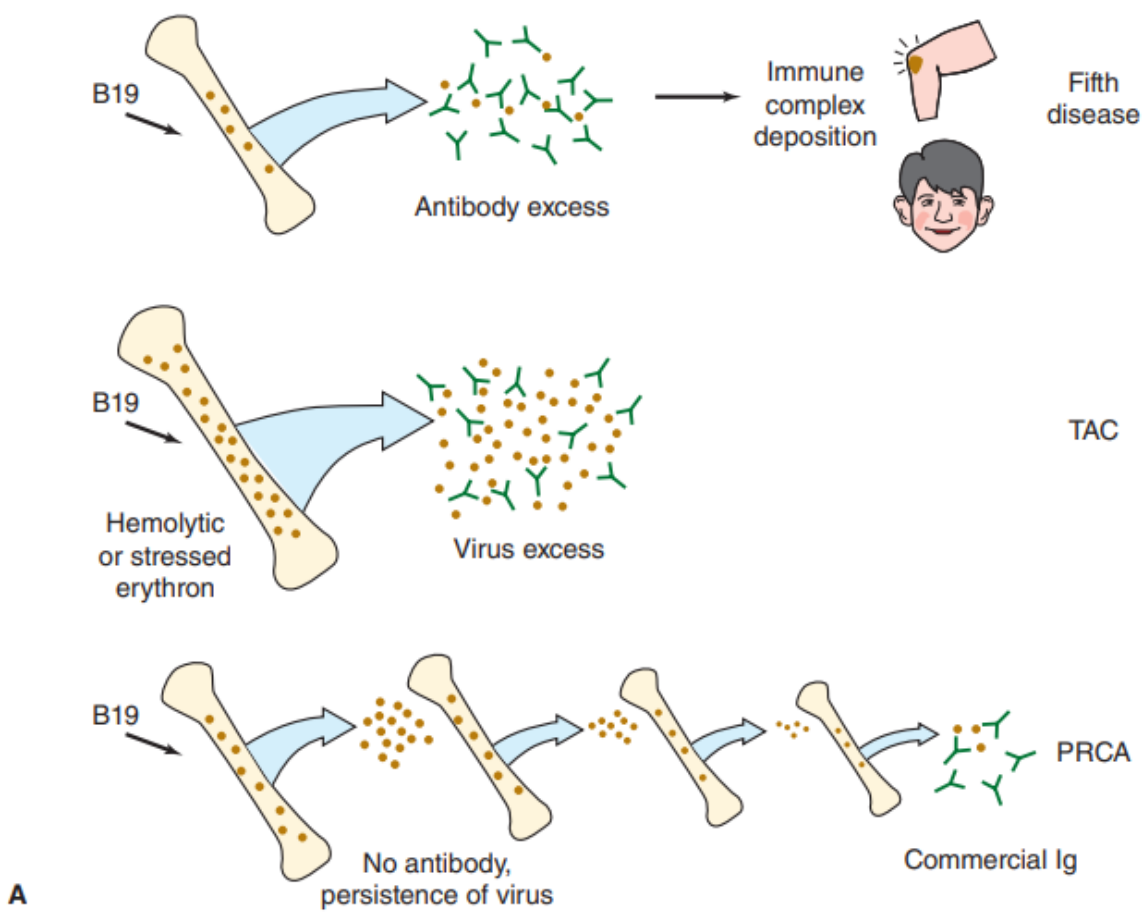
Epidemiology

- The viral infection is common among children 5-15 years old
- Epidemiologic evidence suggests that spread of the virus is primarily by the respiratory route, and high transmission rates occur in households
- Once skin rash appear the virus is no more contagious
- Outbreaks tend to be small and localized, particularly during the spring months, with the highest rates among children and young adults
- Seroepidemiologic studies have demonstrated evidence of past infection in up to 60% of all adults and 90% of elderly people (seropositive IgG)

Pathogenesis



- Viral replication causes cell death interrupting red blood cell production (anemia)
- Bone marrow biopsies from infected patients show erythrocyte maturation arrest, with erythroblast intranuclear inclusions
- Both virus-specific IgM and IgG antibodies are made after B19 infections which form immune complex
- The clinical consequences of the viral effect on erythrocytes are generally trivial, unless patients are already compromised by a chronic hemolytic process, such as sickle cell disease or thalassemia or in immunocompromised patients



1. Erythema infectiosum

2. transient aplastic crisis

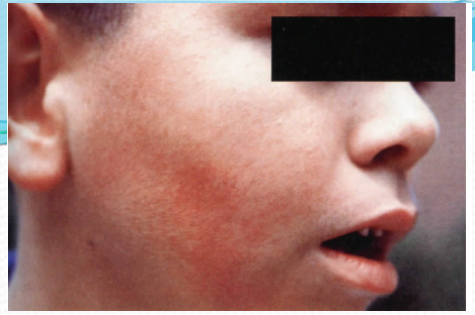
3. pure red cell aplasia

4. Hydrops fetalis

TABLE 31-2 Human Diseases Associated with B19 Parvovirus

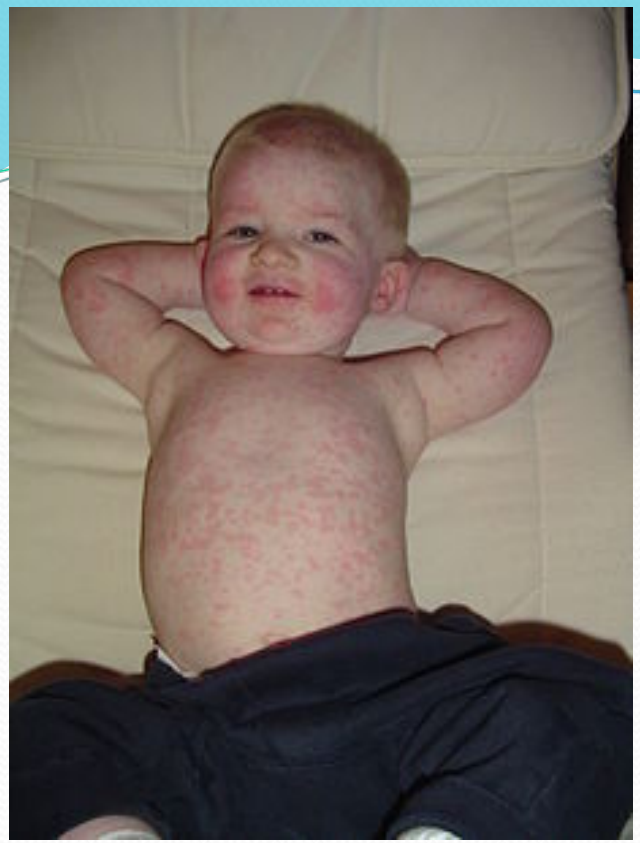
Syndrome	Host or Condition	Clinical Features
Erythema infectiosum	Children (Fifth disease) Adults	Cutaneous rash Arthralgia–arthritis
Transient aplastic crisis	Underlying hemolysis	Severe acute anemia
Pure red cell aplasia	Immunodeficiencies	Chronic anemia
Hydrops fetalis	Fetus	Fatal anemia

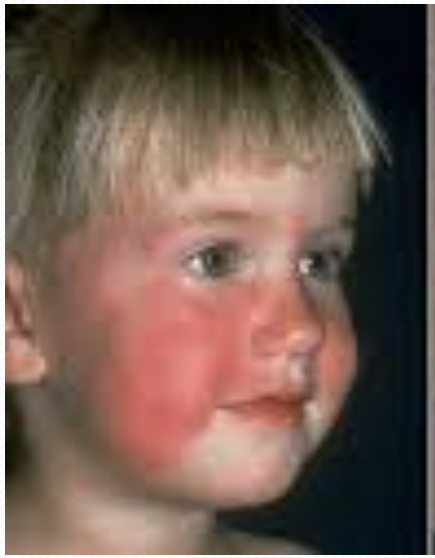
1- Erythema infectiosum

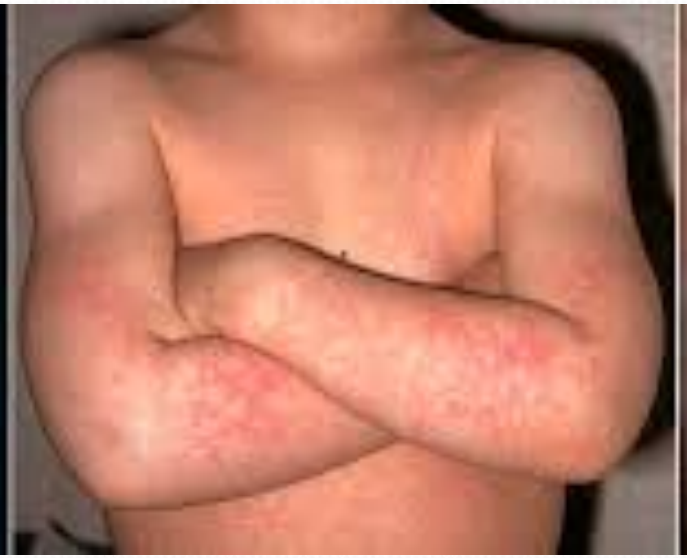


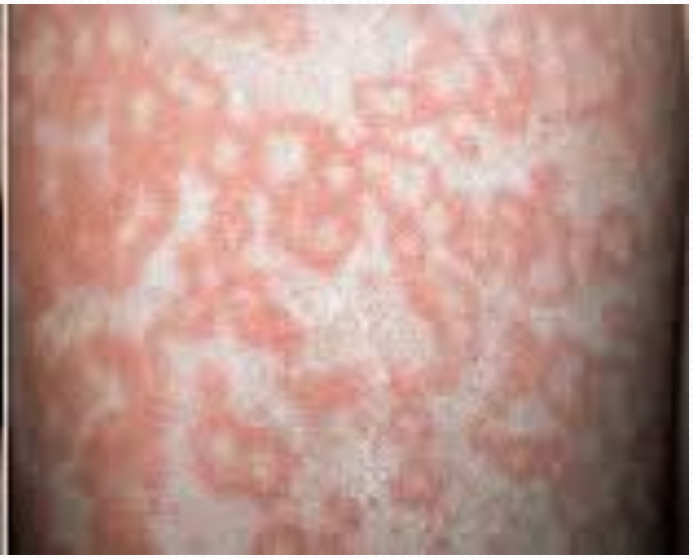
- Erythema infectiosum (also referred to as fifth disease, slapped check, apple face, or academy rash)
- After an incubation period of 4 to 12 days, a mild illness appears, characterized by fever, malaise, headache, myalgia, and itching in varying degrees
- Viremia occurs 1 week after infection and persists for about 5 days
- A confluent, indurated rash appears on the face, giving a “slapped-cheek” appearance. The rash spreads in a day or two to other areas, particularly exposed surfaces such as the arms and legs, where it is usually macular and reticular
- During the acute phase, generalized lymphadenopathy or splenomegaly may be seen, along with a mild leukopenia and anemia

- The illness lasts 1 to 2 weeks, but rash may recur for periods of 2 to 4 weeks thereafter, exacerbated by heat, sunlight, exercise, or emotional stress
- Arthralgia sometimes persists or recurs for weeks to months, particularly in adolescent or adult females
- Serious complications, such as hepatitis, thrombocytopenia, nephritis or encephalitis are rare

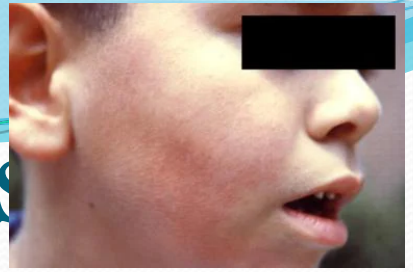






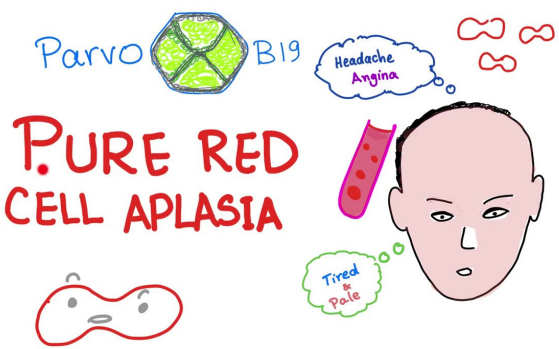


2- Transient Aplastic Crisis



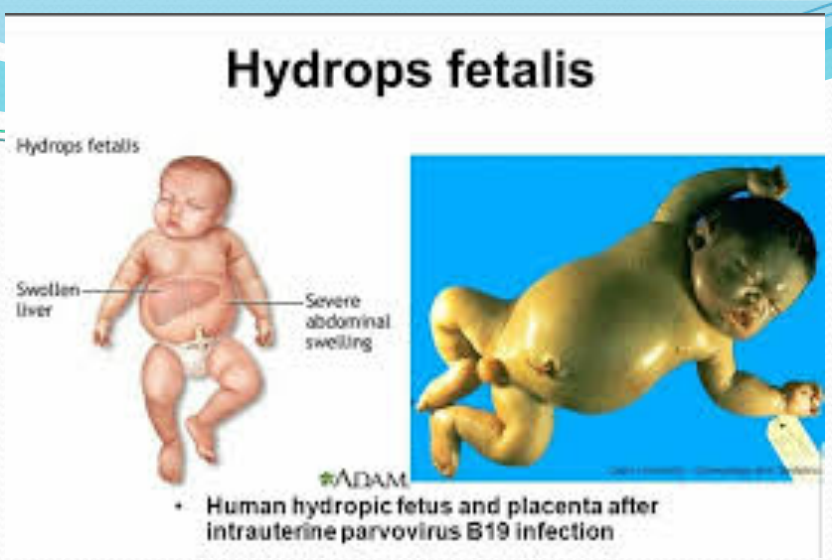
- Transient aplastic crisis may complicate chronic hemolytic anemia (sickle cell disease, thalassemias), acquired hemolytic anemias in adults, and after bone marrow transplantation.
- Abrupt cessation of RBCs synthesis in the bone marrow (reduction of erythroid precursors), accompanied by a rapid worsening of anemia.
- The infection lowers production of erythrocytes, causing a reduction in the hemoglobin level.
- The temporary arrest of production of RBCs becomes apparent only in patients with chronic hemolytic anemia because of the shortened life span of their erythrocytes

3. Pure red cell aplasia



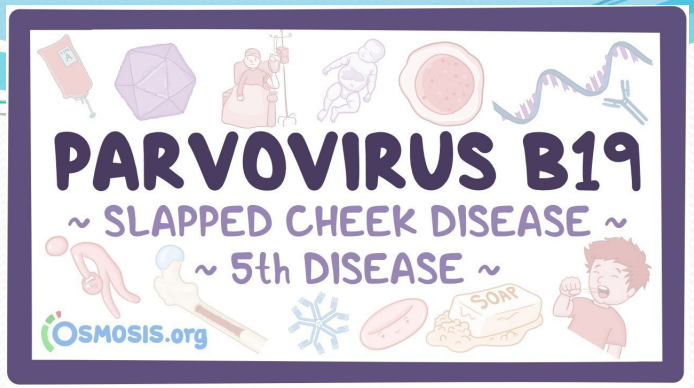
- B19 may establish persistent infections and cause chronic suppression of bone marrow and chronic anemia in immunocompromised patients.
- The disease is called pure red cell aplasia.
- The anemia is severe, and patients are dependent on blood transfusions.
- It has been observed in patient populations with congenital immunodeficiency, malignancies, AIDS, and organ transplantation

4. Hydrops fetalis



- Maternal infection with B19 virus may pose a serious risk to the fetus, resulting in hydrops fetalis and fetal death due to severe anemia.
- The overall risk of human parvovirus infection during pregnancy is low; fetal loss occurs in fewer than 10% of primary maternal infections.
- Fetal death occurs most commonly before the 20th week of pregnancy.

Diagnosis



- Viremia usually lasts 7 to 12 days but can persist for months in some individuals
- CBC (low Hb)
- Polymerase chain reaction (PCR)
- IgM-specific antibody late in the acute phase or during convalescence strongly supports the diagnosis
- Antigen detection assays
- Bone marrow biopsy

Management

- Fifth disease and transient aplastic crisis are treated symptomatically
- Severe anemia due to the latter may require transfusion therapy
- Commercial immunoglobulin preparations contain neutralizing antibodies to human parvovirus. These can sometimes ameliorate persistent B19 infections in immunocompromised patients and in those with anemia
- There is no vaccine against human parvovirus
- There is no antiviral drug therapy