



Medical Virology for 2nd Year M.D. Students

Parvoviruses and Adenoviruses

University of Jordan

School of Medicine

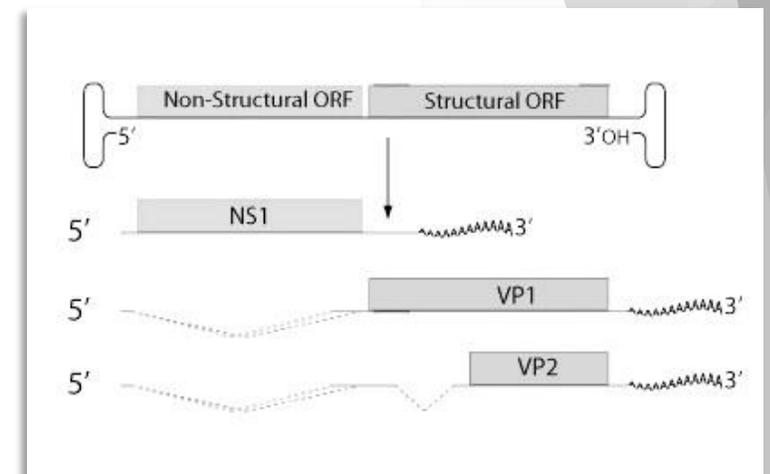
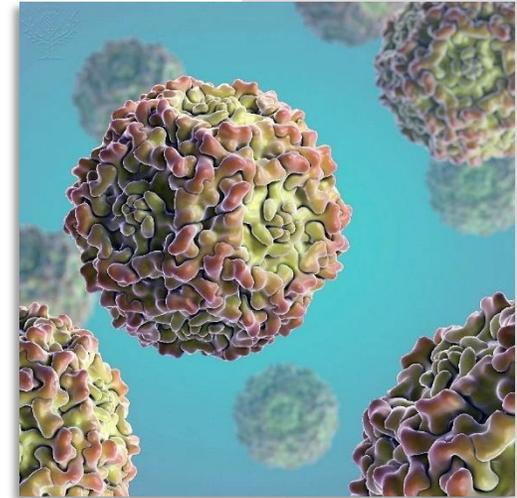
Section of Microbiology & Immunology

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Parvoviruses

- The simplest DNA animal viruses.
- Its replication is dependent on replicating host cells or by co-infecting helper viruses.
- Virions are extremely resistant to inactivation (stable between a pH of 3 and 9 and withstand heating at 56°C for 60 minutes). Virions contain two coat proteins that are encoded by an overlapping, in-frame DNA sequence, so that VP2 is identical in sequence to the carboxy portion of VP1. The major capsid protein, VP2, represents about 96% of virion protein.
- Autonomous parvoviruses usually encapsidate primarily DNA strands complementary to viral mRNA.





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:

Very simple viruses

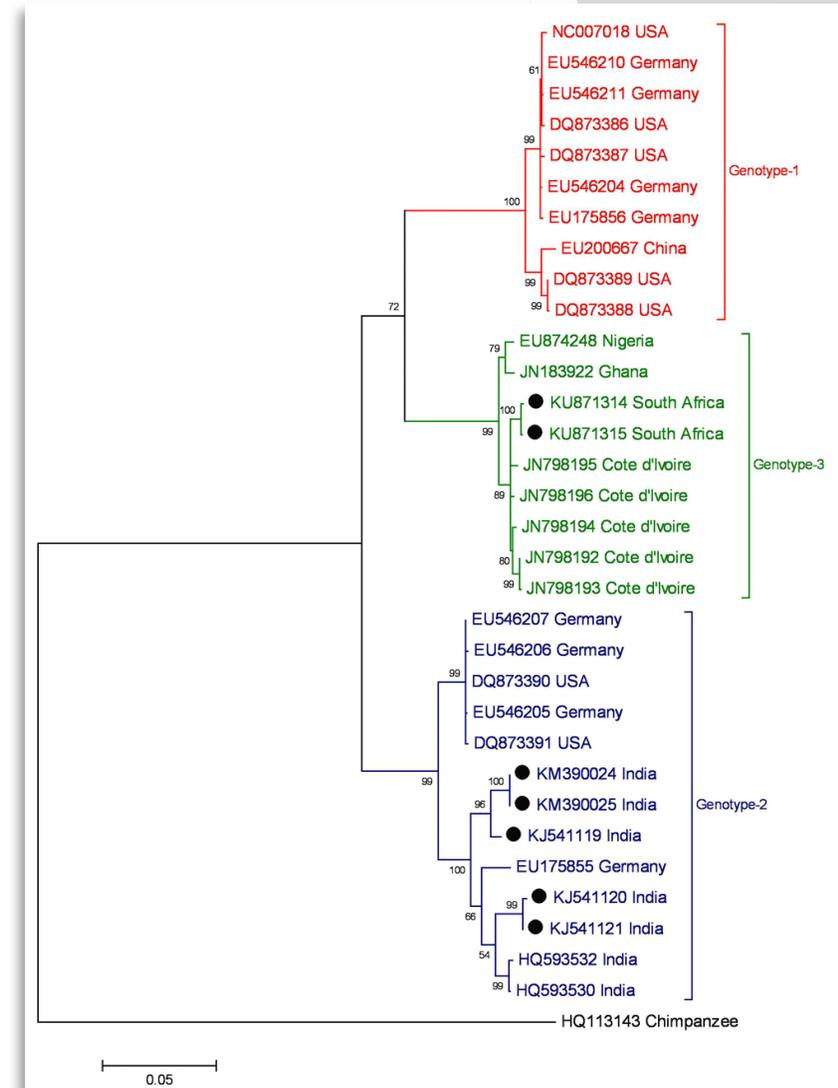
Human pathogen, B19, has tropism for red blood cell progenitors

One genus contains viruses that are replication-defective and require a helper virus



Classification of Parvoviruses

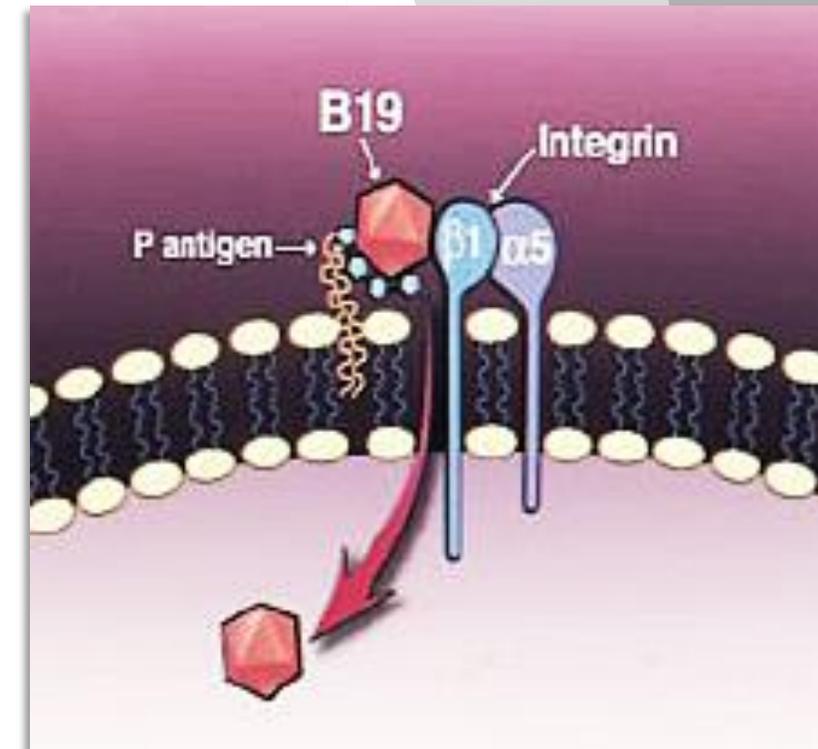
- Subfamilies of *Parvoviridae*: *Parvovirinae* (infect vertebrates) and *Densovirinae* (infect insects).
- *Parvovirinae* comprise five genera. Parvovirus B19 is the most common member of the *Erythrovirus* genus. There are three human genotypes in this genus.
- The three human bocaviruses are in the *Bocavirus* genus.
- The genus *Dependovirus* contains members that are defective and depend on a helper virus (an adenovirus or herpesvirus) for replication.
- Human “adeno-associated viruses” have not been linked with any disease.





Parvovirus Replication

- It is difficult to culture human B19 parvovirus; only primary erythroid progenitors are known to be permissive for B19 infection.
- **The cellular receptor for B19 is blood group P antigen (globoside).** P antigen is expressed on mature erythrocytes, erythroid progenitors, and fetal liver and heart, which helps explain the narrow tissue tropism of B19 virus. **The $\alpha_5\beta_1$ integrin is believed to be a co-receptor for B19 entry.**
- **Viral DNA replication occurs in the nucleus.** They must infect dividing cells with cellular DNA polymerases are involved. The non-structural protein, NS1, is required for virus replication. Viral replication results in cell death.





Human Diseases Associated with B19 Parvovirus

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



Parvovirus Infections in Humans

- Immature cells in the erythroid lineage are targets for B19 parvovirus infection.
- The major sites of B19 virus replication in patients are **adult marrow**, and the **fetal liver**.
- Viral replication causes cell death, interrupting red blood cell production.
- In immunocompromised patients, persistent B19 infections occur, resulting in chronic anemia. In cases of fetal death, chronic infections may have caused severe anemia in the fetus.



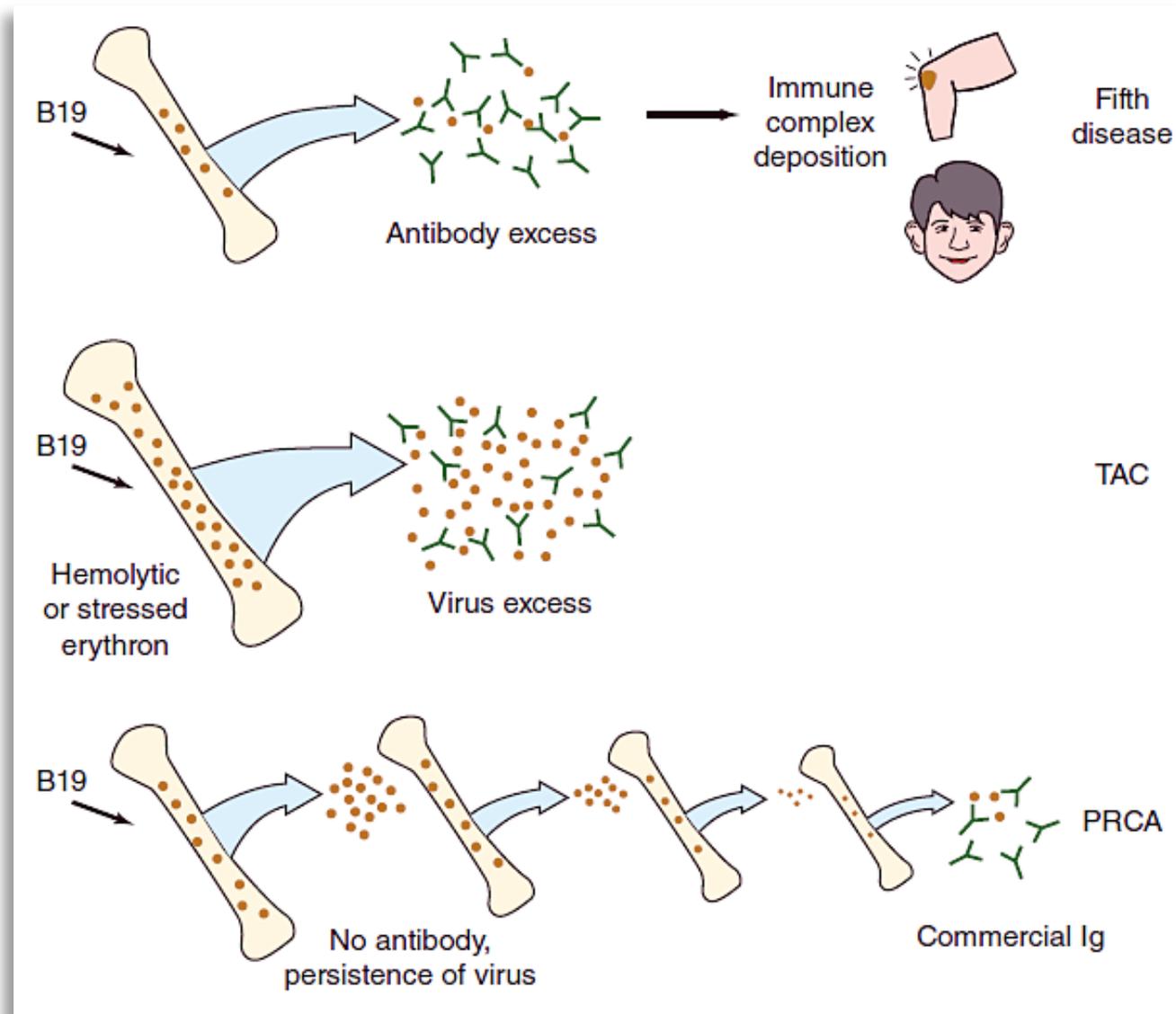
Fetal Liver



Bone Marrow

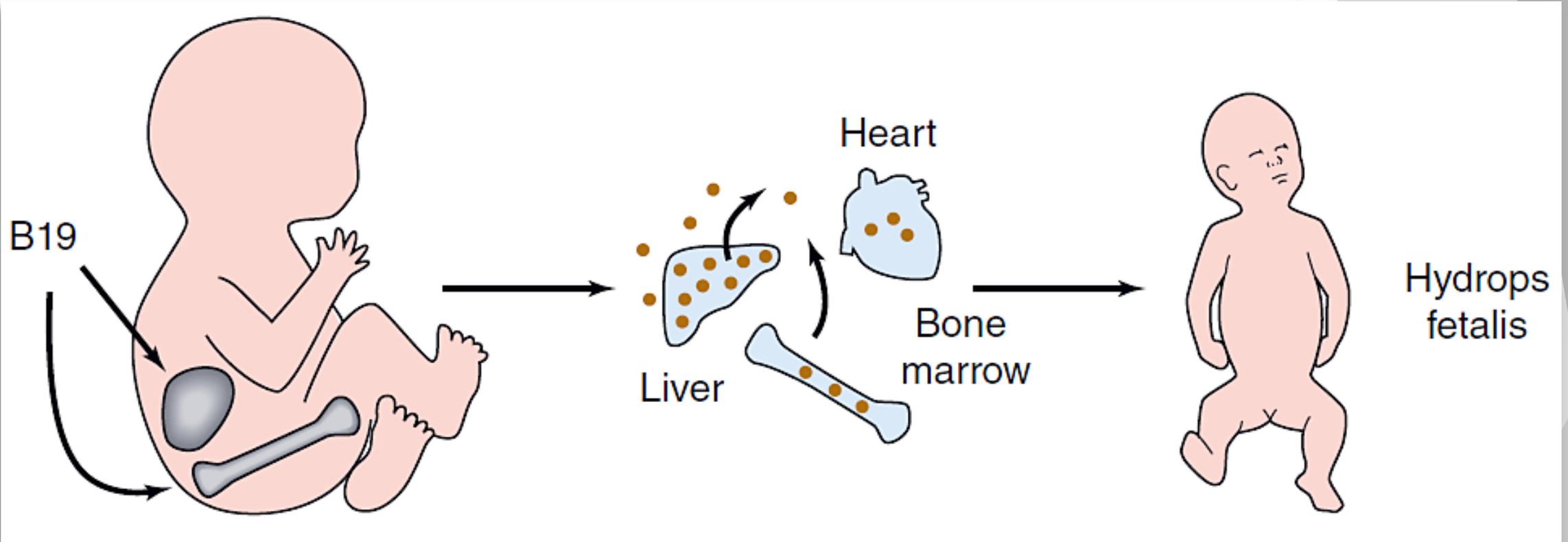


Pathogenesis of B19 Parvovirus Diseases



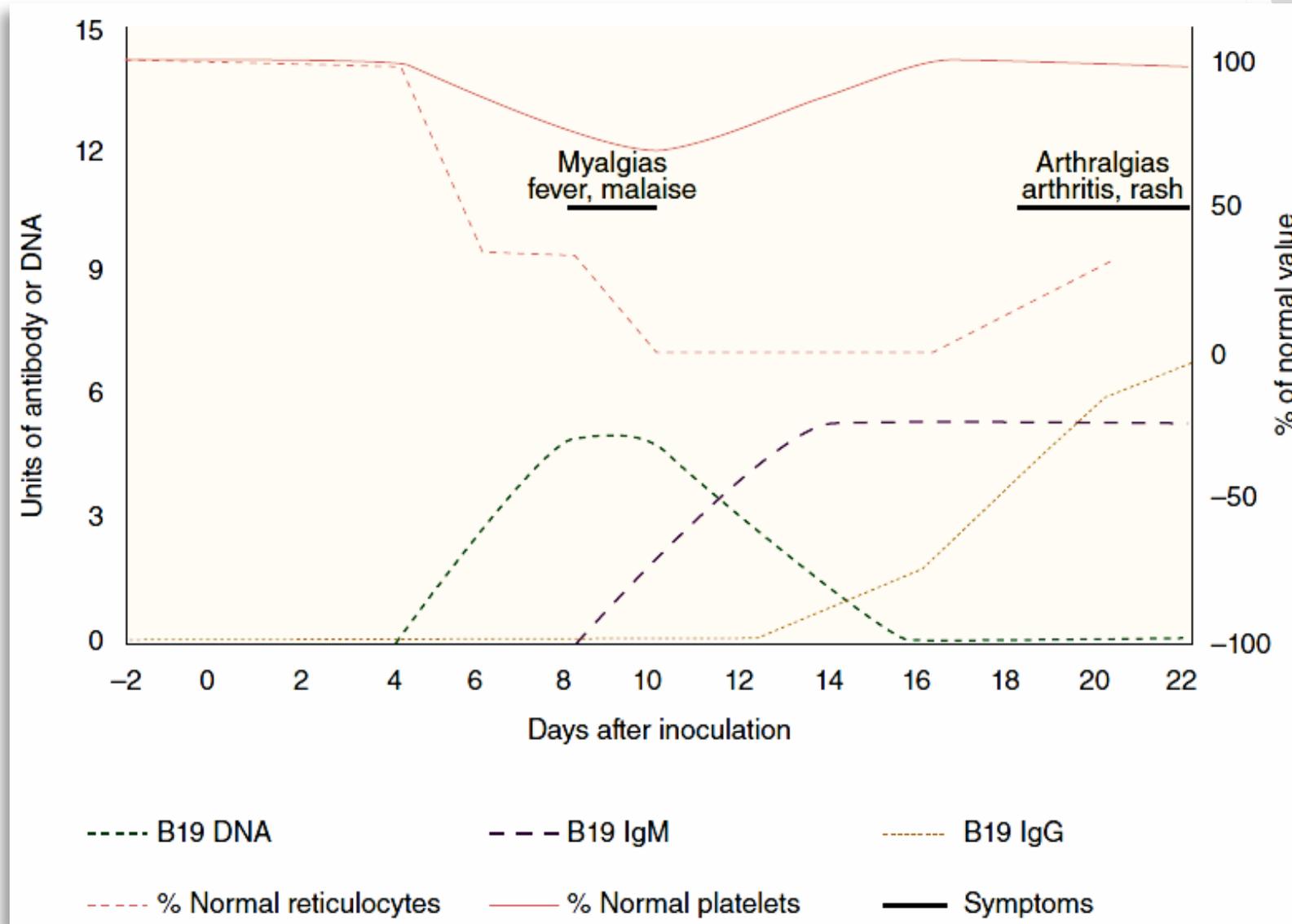


Pathogenesis of B19 Parvovirus Diseases





Clinical and laboratory findings of B19 infection in adult volunteers





Parvovirus B19 Infections in Humans

- Persistent infections occur in patients with immune deficiencies resulting in anemia.
- The rash associated with erythema infectiosum is at least partly immune complex-mediated.
- **Transmission is by the respiratory route.** There is no evidence of virus excretion in feces or urine.
- The virus can also be transmitted parenterally by transfusion and vertically.
- The pathogenesis of human bocavirus infection is not yet known. Because it has been found in respiratory specimens, it is presumed to infect the respiratory tract and be transmitted by the respiratory route. It has also been detected in stool and serum samples.



Clinical Findings

Erythema Infectiosum (Fifth Disease)

- The most common manifestation of B19 infection.
- It is most common in children of early school age and occasionally affects adults, both in sporadic and epidemic forms.
- Mild constitutional symptoms may accompany the rash, which has a typical **“slapped cheek” appearance**.
- **Joint involvement is a prominent feature in adult cases;** joints in the hands and the knees are most frequently affected. The symptoms mimic rheumatoid arthritis, and the arthropathy may persist for weeks, months, or years.





Clinical Findings

Erythema Infectiosum (Fifth Disease)

- The incubation period is usually 1–2 weeks but may extend to 3 weeks.
- Viremia occurs 1 week after infection and persists for about 5 days with the upper respiratory as the site of viral shedding.
- The first phase of illness at the end of the first week include fever, malaise, myalgia, chills, and itching coinciding with viremia and reticulocytopenia and with detection of circulating IgM–parvovirus immune complexes.
- After an incubation period of about 17 days, a second phase of illness begins. The appearance of an erythematous facial rash and a lacelike rash on the limbs or trunk may be accompanied by joint symptoms, especially in adults. The illness is short-lived, with the rash fading after 2–4 days, although the joint symptoms may persist longer. Specific IgG antibodies appear about 15 days post-infection.



Clinical Findings

Transient Aplastic Crisis and Pure Red Cell Aplasia

- Parvovirus B19 is the cause of transient aplastic crisis that may complicate chronic hemolytic anemia, such as in patients with SCD, thalassemias, and AHA in adults or may occur after BMT with absence of erythroid precursors in the marrow, accompanied by a rapid worsening of anemia.
- The temporary arrest of production of red blood cells becomes apparent only in patients with chronic hemolytic anemia because of the short life span of their erythrocytes.
- Symptoms of transient aplastic crisis occur during the viremic phase of infection.
- Persistent infections will cause chronic suppression of BM and chronic severe anemia in immunocompromised patients (congenital immunodeficiency, malignancies, AIDS, and organ transplants), which is called pure red cell aplasia.



B19 Parvovirus Infection During Pregnancy

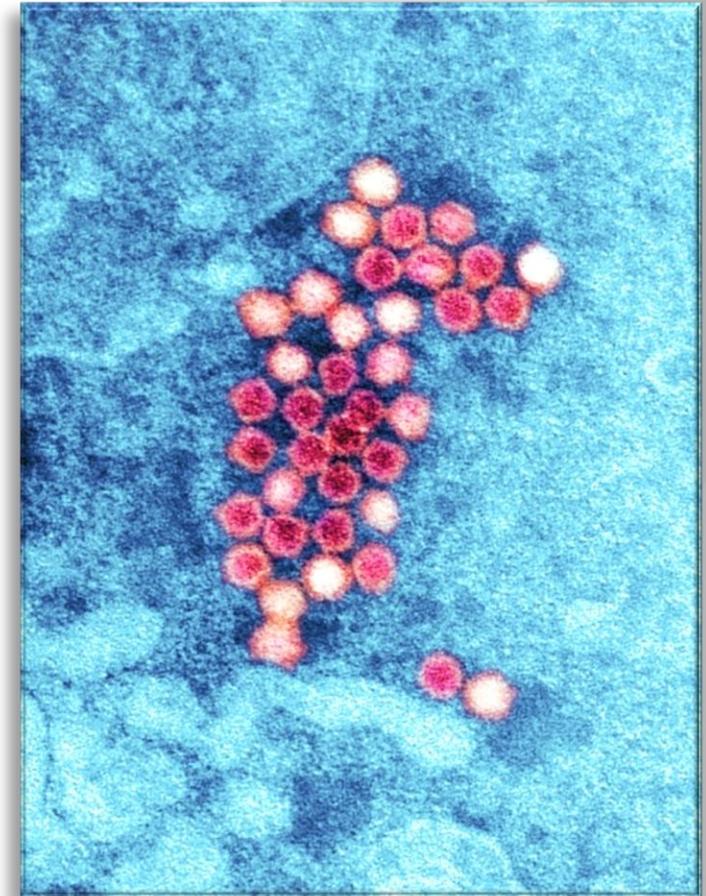


- Maternal infection with B19 virus may result in hydrops fetalis and fetal death due to severe anemia.
- Fetal death occurs most commonly before the 20th week of pregnancy.
- Maternal–fetal transmission may occur most commonly in pregnant women with high plasma viral loads.



Human Bocavirus Respiratory and GI 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.
- The virus has been detected in about 3% of stool samples from children with acute gastroenteritis.
- Co-infection rates with other enteric pathogens were high, so any causative role of bocavirus in gastroenteritis is unknown.





Laboratory Diagnosis of Parvovirus Infections

- The most sensitive tests detect viral DNA.
- Available tests are PCR, probe hybridization of serum or tissue extracts, and in situ hybridization of fixed tissue. **PCR is the most sensitive assay.**
- B19 DNA has been detected in serum, blood cells, tissue samples, and respiratory secretions. During acute infections, viral loads in the blood can reach approximately 10^{11} genome copies/mL.
- The only assay currently available for human bocavirus is PCR. Bocavirus DNA has been found in serum, saliva, stool samples, and respiratory specimens.



Laboratory Diagnosis of Parvovirus Infections

- Serologic assays based on recombinant parvovirus B19 antigens are used to measure antibodies. VP2 virus-like particles appear to be optimal as antigen for antibody detection. Detection of B19 IgM antibody is indicative of recent infection; it is present for 2–3 months after infection.
- B19 IgG antibody against conformational epitopes on VP1 and VP2 persists for years, although antibody responses against linear epitopes decline within months post-infection. Antibody may not be found in immunodeficient patients with chronic B19 infections. In those patients, chronic infection is diagnosed by detecting viral DNA.
- Antigen detection assays can identify high-titered B19 virus in clinical samples. Immunohistochemistry has been used to detect B19 antigens in fetal tissues and bone marrow.
- B19 and bocaviruses are difficult to grow. Virus isolation is not used to detect infection.



Epidemiology of Parvovirus Infections

- The B19 virus is widespread. Infections can occur throughout the year in all age groups.
- Up to 60% of all adults and 90% of elderly people are seropositive.
- B19 infection is transmitted via the respiratory tract. Transfer among siblings and children in schools and daycare centers is the main path of transmission.
- Many infections are subclinical.
- Whereas patients with aplastic crisis are likely to be infectious during the course of their illness, patients with fifth disease are probably no longer infectious by the time of onset of rash.
- The epidemiology of human bocavirus is not known. It has been found in young children and appears to be global in distribution.



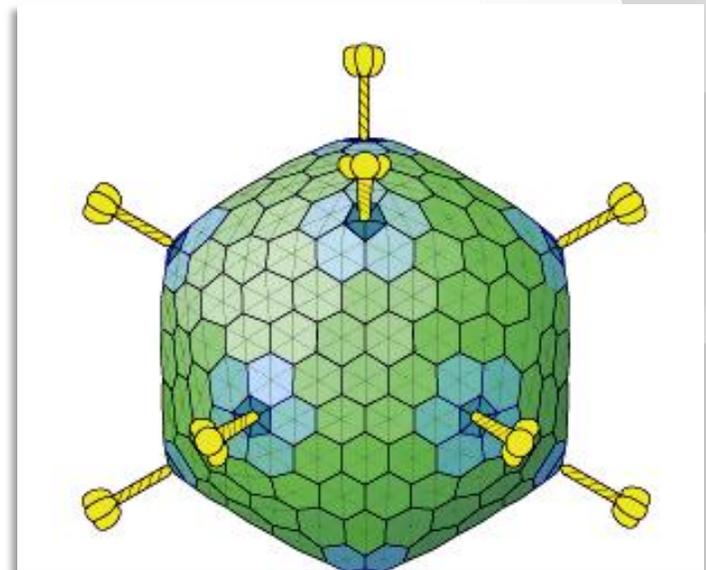
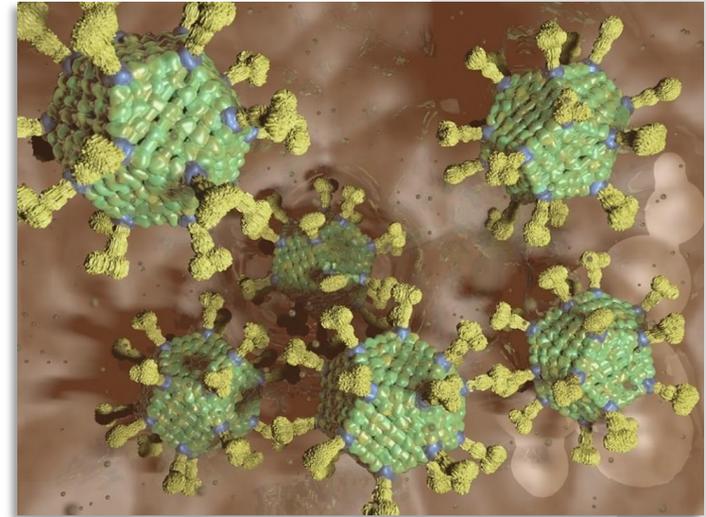
Treatment, Prevention and Control of Parvovirus Infections

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



Adenoviridae-Introduction

- First found in adenoid tissue (tonsils).
- Naked viruses.
- Icosahedral
- Contain double-stranded DNA genome.
- At the 12 vertices of the capsid, fibers that contain type-specific antigens are protruding which are important in serotyping.





Adenovirus (Ad)-Classification

- There are 57 serotypes in the seven species of human Ads:
 - species A (Ad12, 18, 31).
 - species B (Ad3, 7, 11, 14, 16, 34, 35, 50, 55).
 - species C (Ad1, 2, 5, 6).
 - species D (Ad8 to 10, 13, 15, 17, 19, 20, 22 to 30, 32, 33, 36 to 39, 42 to 49, 51, 53, 54, 56).
 - species E (Ad4).
 - species F (Ad40 and 41).
 - species G (Ad52).



Adenovirus-Pathogenesis

- Adenoviruses infect and replicate in epithelial cells of the respiratory tract, eye, gastrointestinal tract and urinary bladder.
- Usually, adenoviruses cause localized infection and do not spread systemically.
- Most human adenoviruses replicate in intestinal epithelium after ingestion but usually produce subclinical infections rather than overt symptoms.

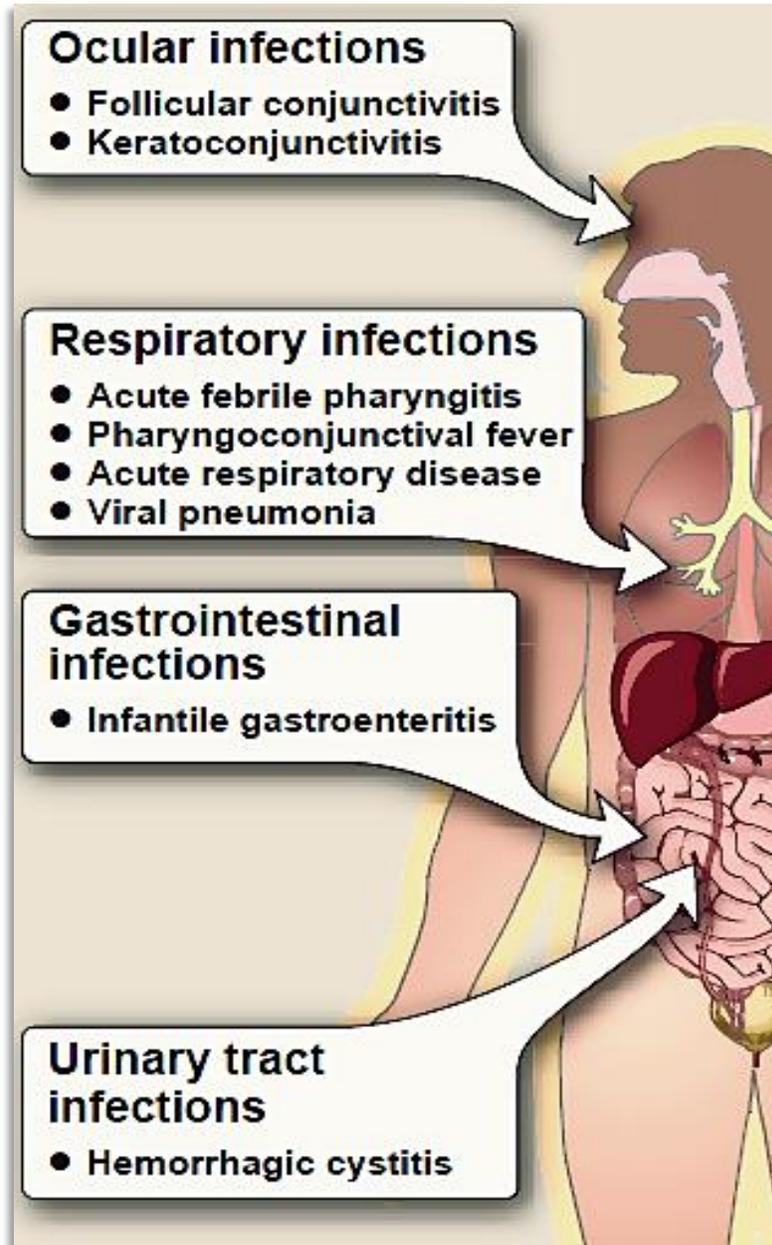


Adenovirus-Transmission

- The site of the clinical syndrome caused by an adenovirus infection is generally related to the mode of virus transmission.
- Most adenoviruses are primarily agents of respiratory disease, which are transmitted via the respiratory route. The GI disease is transmitted via the fecal-oral route.
- Similarly, ocular infections are transmitted by direct inoculation of the eye by virus-contaminated hands, ophthalmologic instruments, or bodies of water in which groups of children swim together.



Adenovirus-Summary of clinical features





Adenovirus-Respiratory Disease

- The most common manifestation of adenovirus infection of infants and young children is acute febrile pharyngitis, characterized by a cough, sore throat, nasal congestion, and fever.
- Some adenovirus types tend additionally to produce conjunctivitis, in which case the syndrome is referred to as pharyngoconjunctival fever.
- Adenoviruses are thought to be responsible for about 10–20% of pneumonias in childhood.
- Adenoviral pneumonia has been reported to have an 8–10% mortality rate in the very young.





Adenovirus-Ocular Disease

- In addition to the conjunctivitis that accompanies the upper respiratory infection, a similar condition may occur as a separate disease. It is self-limiting and has no permanent sequelae.
- A more serious infection is epidemic keratoconjunctivitis, which involves the corneal epithelium, and may be followed by corneal opacity lasting several years.
- The epidemic nature of this disease results from transmission via shared towels or ophthalmic solutions, person-to-person contact, or improperly sterilized ophthalmologic instruments.



Adenovirus-GI Disease

- Most human adenoviruses multiply in the GI tract and can be found in stools; however, these are generally asymptomatic infections.
- Two serotypes (types 40 and 41) have been associated specifically with infantile gastroenteritis and may account for 5–15% of cases of viral gastroenteritis in young children.
- Clinical manifestations include: Long-lasting diarrhea, less frequent vomiting, frequent development of dehydration, and abdominal pains and distension.



Acute Hemorrhagic Cystitis

- An illness that is associated with Ad11.
- Characterized by gross hematuria.
- Its significance lies in the potential confusion with other, more serious diseases of the kidney (such as glomerulonephritis).
- This self-limited disease is usually not accompanied by fever or hypertension, and tests of renal excretory and concentrating functions have been essentially normal.



Epidemiology, Diagnosis, Treatment and Prevention



- Adenoviruses exist in all parts of the world and they are present year round. The most common serotypes in clinical samples are the low-numbered respiratory types (1, 2, 3, 5, and 7) and the gastroenteritis types.
- Dx: Ag detection or PCR.
- There is no specific treatment for adenovirus infections.
- Careful hand washing is the easiest way to prevent infections.
- Live adenovirus vaccine containing types 4 and 7 is available.



Thanks for listening