

# 血 Hematology 血



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● Dr. name :  
Dr Sameer

● Lecture number :  
Parvovirus

● Done BY :





# Medical Virology

## Parvoviruses

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# Parvoviruses – Introduction

- Parvoviruses are very small (18 to 26 nm), naked virions that contain a linear single stranded DNA molecule.
- Diseases caused by parvoviruses have been recognized among nonhuman hosts for a number of years. Notable among these are canine parvovirus and feline panleukopenia virus, which produce particularly severe infections among puppies and kittens, respectively. These do not appear to cross species barriers.
- The human parvovirus B19 has been well described, but its origin is not yet known.

# Properties of Parvoviruses

- Structure
  - Icosahedral
  - 18-26 nm diameter
  - Single-stranded DNA, 5.6 kb
  - Two proteins
  - Nonenveloped (Naked virus)
- Classification
  - *Parvoviridae* (vertebrates)
    - ***Parvovirus***
    - *Erythrovirus*
    - *Dependovirus* (requires **helper virus**, such as an adenovirus)
  - *Densovirinae* (insects)

- Parvovirus B19 encodes three capsid proteins (VP1, VP2, and VP3). The virus can be grown in primary cultures of human bone marrow cells, fetal liver cells, hematopoietic progenitor cells generated from peripheral blood, and a megakaryocytic leukemia cell line.
- The major cellular receptor for the virus is globoside (also known as blood group **P antigen**, which is commonly found on erythroid progenitors, erythroblasts, megakaryocytes, and endothelial cells). All represent potential targets for disease production.
- A primary site of replication appears to be the nucleus of an immature cell in the erythrocyte lineage. Such infected cells then cease to proliferate, resulting in an impairment of normal erythrocyte development.

- Parvovirus B19 infection is common worldwide, and most persons who contract the virus are infected by 15 years of age. Infection is most common in late winter or early spring.
- The virus is transmitted through exposure to infected respiratory droplets or blood products and vertically from mother to fetus. Exposure to respiratory droplets is the most common means of transmission. The transmission rate is about 50 percent for those living with infected persons and about 20 to 30 percent for susceptible teachers and day care workers who are exposed to infected children.
- Nosocomial transmission also has been documented. The incubation period of the infection ranges from four to 14 days but can last as long as 21 days.
- Persons with B19 infection are no longer contagious when the rash appears because viremia has cleared by this point. Most symptoms occur secondary to immune complex formation.

# Parvovirus Infections in Humans

- Diseases
  - **Fifth disease** (cutaneous rash)
  - **Arthralgia**
  - **Transient aplastic crisis** (severe acute anemia)
  - **Pure red cell aplasia** (chronic anemia)
  - **Hydrops fetalis** (fatal fetal anemia)
  - **B19 virus** most common
- Fifth Disease (Erythema infectiosum or Academy rash)
  - Targets **red blood cell progenitors**
  - **Pain in joints**
  - Results in lysis of cells, thus **depleting** source of mature red cells
  - Anemia ensues
  - Rarely fatal and without complications



Fifth Disease (parvovirus B19)

- Transient aplastic crisis
  - B19 infection of those with other hemolytic anemias
    - Sickle cell disease
    - Thalassemias
  - Can complicate crises
  - **Sometimes fatal**
- Infection of immunodeficient patients
  - Can cause **persistent infection** in bone marrow
  - Suppress red cell maturation
  - Leads to anemia
- Infection during pregnancy
  - Can cause **fetal anemia**
  - Usually not fatal to fetus



# Clinical Conditions Associated with Parvovirus B19

- Most persons with parvovirus B19 infection are symptomatic or exhibit mild, nonspecific, cold-like symptoms that are never linked to the virus. However, clinical conditions associated with the infection include erythema infectiosum; arthropathy; transient aplastic crisis; chronic red cell aplasia; papular, purpuric eruptions on the hands and feet (“gloves and socks” syndrome); and hydrops fetalis.
- Conditions postulated to have a link to parvovirus B19 infection include encephalopathy, epilepsy, meningitis, myocarditis, dilated cardiomyopathy, and autoimmune hepatitis.

# ERYTHEMA INFECTIONOSUM (FIFTH DISEASE)

- Erythema infectiosum is the most recognizable presentation of parvovirus B19 infection.
- The disease generally affects children four to 10 years of age although a less-pronounced rash can occur in adults. Prodromal symptoms are mild and include fever, coryza, headache, and nausea.
- The first stage of the rash *presents as erythema of the cheeks* (“slapped-cheek” rash) with circumoral pallor.
- After one to four days, the second stage *appears as a maculopapular rash of the extremities* and trunk. Central clearing of the rash is possible, giving it a lacy, reticular pattern. The second-stage rash usually lasts one to six weeks.
- The third stage may continue for the next one to three weeks. The rash persists but varies with exposure to heat or sunlight, resolving spontaneously with no permanent sequelae.

# ARTHROPATHY

- Arthropathy may be a complication of erythema infectiosum or a primary presentation of parvovirus B19 infection.
- Approximately 8 percent of children infected with the virus have arthralgia. However, arthralgia is more common in adolescents and adults with parvovirus B19 infection, affecting up to 60 percent of these persons.
- Arthropathy affects women twice as often as men.
- Arthropathy generally resolves within three weeks but can last for months to years, especially in women. In children, the pattern can be symmetric or asymmetric and usually involves the knees (82 percent of patients) and ankles. Some patients may test positive for rheumatoid factor and antinuclear antibodies.

# TRANSIENT APLASTIC CRISIS

- Persons with decreased erythrocytes caused by conditions such as iron deficiency anemia, human immunodeficiency virus (HIV), sickle cell disease, spherocytosis, or thalassemia are at risk of transient aplastic crisis if infected with parvovirus B19. The virus causes a cessation of erythrocyte production. This can be life threatening, although most patients make a full recovery within two weeks.
- Multiple blood transfusions may be necessary initially. The precipitous drop in hemoglobin also may cause congestive heart failure, a cerebrovascular accident, or acute splenic sequestration.
- White blood cell and platelet counts also may fall.<sup>11</sup> Patients are highly contagious during aplastic crisis and should be isolated to prevent transmission of the virus.

# CHRONIC RED CELL APLASIA

- Parvovirus B19 infection may persist in immunocompromised persons without antibodies.
- Rashes and arthropathy do not develop because they occur secondary to antibody complex deposition in the skin and joints.
- Patients present with fatigue and pallor caused by anemia, which can be severe, prolonged, or recurrent.
- Reticulocytes may be absent and transfusions may be required.
- If severe anemia continues, intravenous immune globulin treatment may be necessary.

# GLOVES AND SOCKS SYNDROME

- Parvovirus B19 has been associated with papular, purpuric gloves and socks syndrome, although a causative relationship has not been proven.
- The syndrome typically occurs in young adults and presents as symmetric, painful erythema and edema of the feet and hands. The condition gradually progresses to petechiae and purpura and may develop into vesicles and bullae with skin sloughing.
- A hallmark of the syndrome is a sharp demarcation of the rash at the wrists and ankles, although other areas (e.g., cheeks, elbows, knees, inner thighs, glans penis, buttocks, or vulva) may be involved.
- Gloves and socks syndrome also has been associated with hepatitis B, cytomegalovirus, Epstein-Barr virus, human herpesvirus 6, measles, coxsackievirus B, and drug reactions

# HYDROPS FETALIS

- Pregnancy does not alter parvovirus B19 infection in the mother, although the fetal liver and heart may become infected.
- The infant may develop severe anemia, caused by an already shortened red cell lifespan, or may develop myocarditis from direct infection of the heart. The combination of severe anemia and myocarditis can cause congestive heart failure and hydrops fetalis.
- The estimated risk of transplacental infection is 30 percent. Many fetuses are born without symptoms, but there is a 2 to 6 percent risk of fetal loss.
- Second-trimester pregnancies are the most vulnerable because of increased hematopoiesis in the liver. Although the placenta has an abundance of P antigen receptors for the virus, first-trimester pregnancies have the lowest risk because of the fetal inability to produce immunoglobulin M (IgM) and the difficulty of antibody transfer across the placenta.

# Laboratory Diagnosis

- If erythema infectiosum is present, a clinical diagnosis can be made without laboratory testing.
  - PCR is most sensitive
    - Most useful during **viremia**
    - Otherwise, requires **tissue biopsy or bone marrow tap**
  - Serological testing for IgM
    - Determines recent infection (recommended to diagnose acute viral infection in immunocompetent patients).
    - IgG testing is not informative
- Giant pronormoblasts on a peripheral blood smear or in a bone marrow aspirate are suggestive of parvovirus B19 infection but are not diagnostic.



# Epidemiology

- B19 virus is common and widespread
- Most adults have been infected
  - Most infections are **subclinical**
  - IgG is detectable in most healthy people
- Sporadic outbreaks, usually among children, occur each year
- Transmission from **patient to health care staff** is not uncommon
  - Role in **nosocomial** transmission to other patients

# Treatment

- Generally, erythema infectiosum is self-limited and does not require treatment.
- Patients with arthralgia may require nonsteroidal anti-inflammatory drug treatment.
- Patients in transient aplastic crisis may require erythrocyte transfusions while the marrow recovers.
- Chronic red cell aplasia, if severe, may require intravenous immune globulin therapy. This treatment may improve anemia symptoms, but it may precipitate a rash or arthropathy.
- Intravenous immune globulin also has been used in several case reports of severe illness.
- A vaccine has been developed but is not yet available