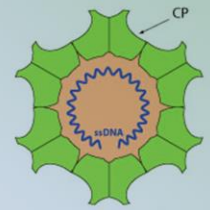
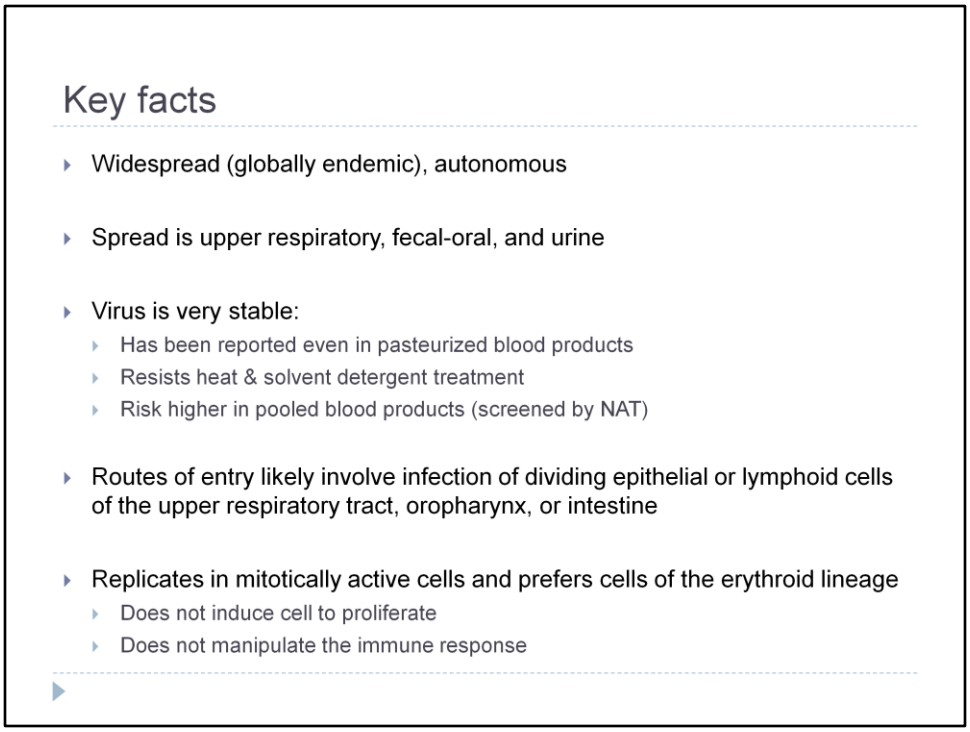


Parvovirus B19

Dr. Mazin Al-Salihi



Other members of the parvovirus family will not be considered, they are dependoviruses (require co-infection with adenovirus for example) and are non-pathogenic.

Major route is probably upper respiratory, rarely also through blood, transplacentally

NAT = nucleic acid testing including but not limited to PCR rtPCR to detect viral titers

Major sites of replication have been assumed to be adult marrow and fetal liver (sites of erythropoiesis)

Associated diseases

- Fifth disease
- Arthropathy
- Transient aplastic crisis in patients with hemolytic disorders
- Chronic pure RBC aplasia in immunocompromised individuals
- Non-immune hydrops fetalis, intrauterine fetal death, or miscarriage

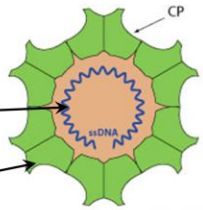
Most B19V infections are asymptomatic or associated with mild non-specific illness

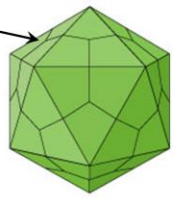
Fetus is highly susceptible to infection owing to the large number of dividing cells. Maternal immunity completely protects the fetus, so primary infection is the problem here.

Molecular Biology

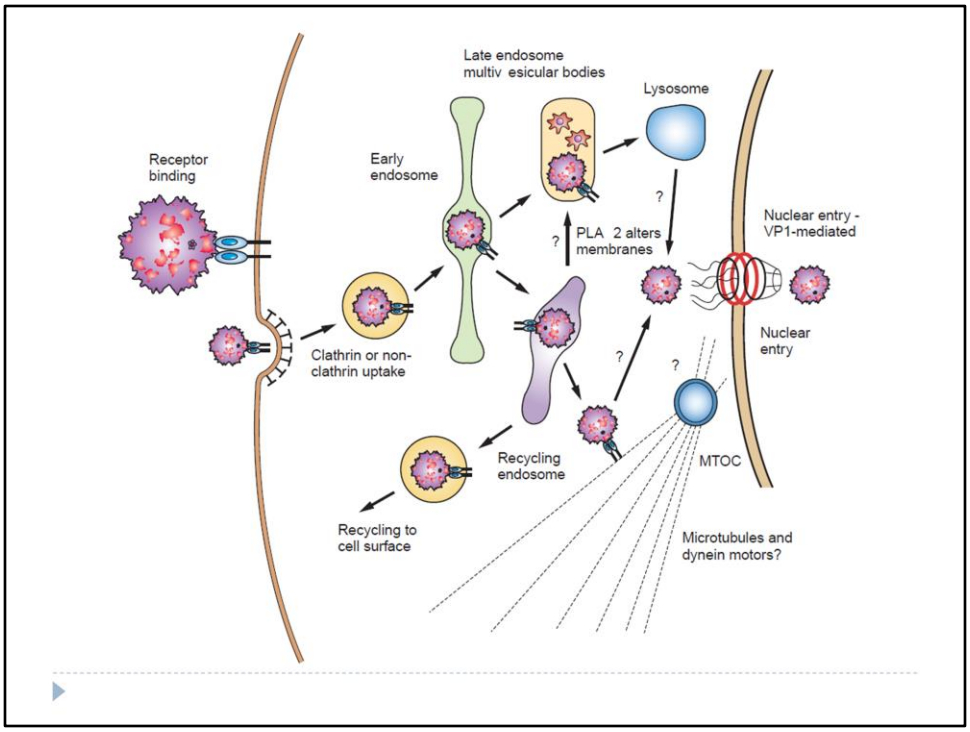
Structure

- Simple structure
- Small ssDNA genome with few genes
- Icosahedral capsid
- Absence of a lipid envelope and small genome produces a very stable viral particle





Icosahedral means twenty faces



Receptor is Globoside “P” antigen of blood which is present mostly on the erythroid progenitor cells, integrin co-receptor

Rare individuals who lack P antigen are resistant to infection with parvovirus

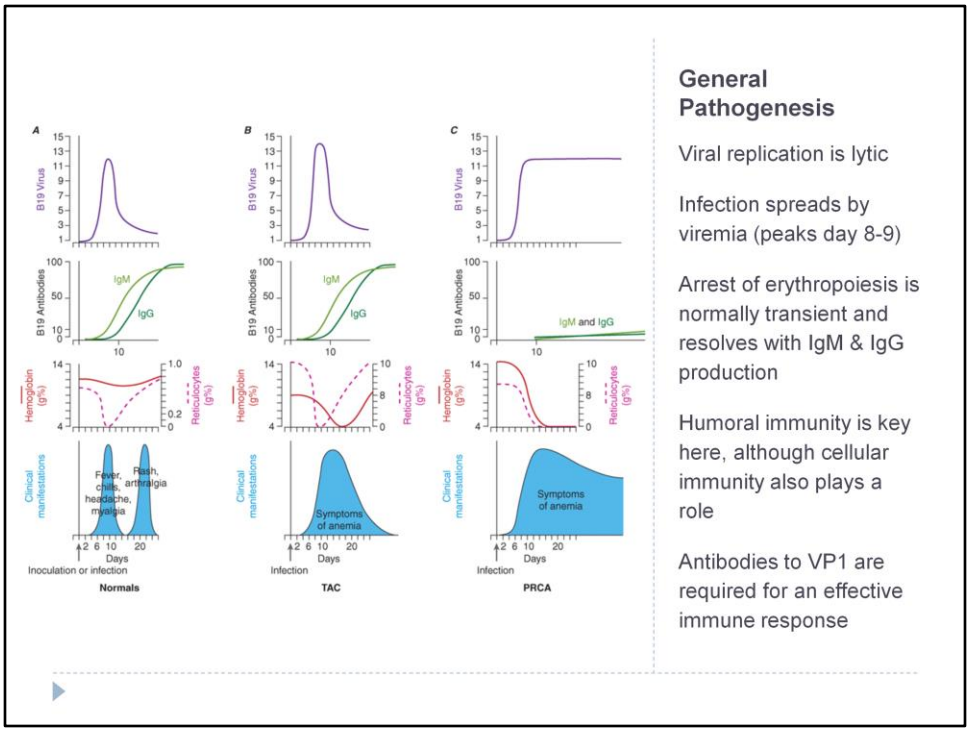
Exact mechanisms of intracellular trafficking unclear

VP1 is one of the proteins that make up the capsid, and its PLA2 activity seems to be required for escape from the endocytic vesicles to the cytoplasm

Some experiments have shown that inhibiting microtubule formation and dynein function reduced intracellular virus trafficking to the nucleus

Viral DNA replication, RNA transcription, protein translation, and virus capsid assembly all occur in the cell's nucleus

Globoside is also found to a lesser extent on other cell types, including endothelial cells, cardiomyocytes, megakaryocytes, and placental trophoblast cells. The globoside-containing, non-erythroid cell types that become infected with B19 produce little if any infectious virus. However, these nonproductive infections may contribute to disease through the expression of nonstructural (NS1) protein, which can induce cellular apoptosis in both permissive and non-permissive cells



Spread is by viremia which starts at day 5 to 6 and peaks at 8 to 9 days.

BM supression coincides with peak lasts 5-7 days, and virus is released into oral and respiratory secretions

Mention bi-phasic. Phase one with viremia non-specific flu like symptoms. Phase two with immune response.

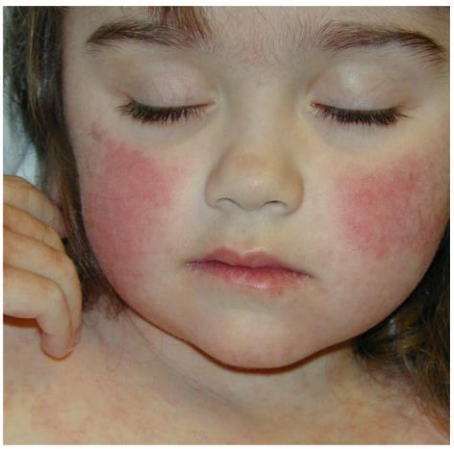
Protective, long- lasting antibody is produced.

PRCA = Chronic anemia/pure red cell aplasia happens when no antibody response is mounted (e.g. immunocompromised, or fetal transmission)

Clinical Syndromes

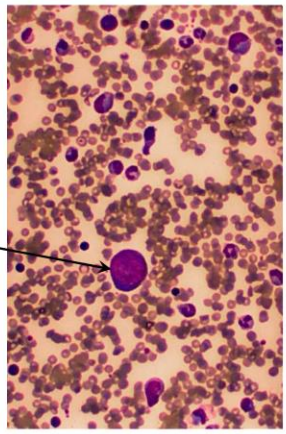
Erythema Infectiosum (fifth disease, slapped cheek syndrome)

- Bi-phasic:
  - Minor febrile prodrome ~7-10 days after exposure
  - Classic facial rash develops after 2-3 days
- Erythematous macular rash may spread to the extremities in a lacy reticular pattern
- Adults may present with arthralgia w w/o rash, rarely with "slapped cheeks"
  - Symmetrical
  - Typically small joints
  - Can mimic RA



Transient Aplastic Crisis

- Precipitous worsening of anemia in patients with a shortened RBC life span and reduced erythropoiesis e.g.:
  - Sickle cell (can precipitate a CVA)
  - Thalassemias
  - Acquired hemolytic anemia
- Characterized by reticulocytopenia, absent erythroid precursors in BM & giant pronormoblasts
- Often associated with variable degrees of neutropenia and thrombocytopenia
- Symptoms are typical of severe anemia
- Can be life threatening, treated with transfusion



From the name it is self limiting but the patient is acutely ill

dyspnea, fatigue, extreme lassitude, confusion, and heart failure

Chronic infection (Pure red cell aplasia)

- Immune supression - failure to mount a neutralizing Ab response
  - Congenital immunodeficiency
  - AIDS
  - Lymphoproliferative disorders (especially acute lymphocytic leukemia)
  - Transplantation
- No immune complex mediated symptoms of fifth disease
- Persistent anemia with reticulocytopenia & scattered giant pronormoblasts in BM
- Rarely, transient neutropenia, lymphopenia, and thrombocytopenia
- Patient is dependent on transfusions

Fetal infection

- Erythroblasts in the fetal liver are infected (30% of maternal infections are vertically transmitted)
- Severe anemia leading to high output cardiac failure
- Highest risk for death in first 2 trimesters
- Fetal infection may persist after birth as pure red cell aplasia

Diagnosis

- Detection of IgM antibodies
  - At time of rash in erythema infectiosum
  - By day 3 in TAC patients
  - Remain detectable for ~3 months
- IgG is detectable by day 7 of illness and persists throughout life
- PCR is most specific and detectable earlier than serology or in chronic infections

Treatment

- No antiviral is available
- Symptomatic treatment
- IVIg for those not capable of an immune response (not useful in EI)
- Intrauterine blood transfusion can prevent fetal loss in some cases of fetal hydrops