Parvovirus B19 Infections
Pathogenesis

- Autonomous parvoviruses are highly parasitic because of their molecular simplicity.

- Parvovirus B19 replicates in mitotically active cells and prefers cells of the erythroid lineage.

- The human parvovirus B19 receptor has been identified as globoside, the blood group “P” antigen.

- Major sites of replication have been assumed to be adult marrow and fetal liver (sites of erythropoiesis).
The absence of lipid envelope and the small DNA content contribute to the high heat stability of parvoviruses.

B19 virus has been transmitted in pasteurized blood products and the virus resists solvent detergent treatment.

The major route of transmission is probably the upper airway, but can be transmitted by contaminated blood products and transplacentally.
Spread is by viremia which starts at day 5 to 6 and peaks at 8 to 9 days.

High titers (10^{14}/ml) are reached and virus is released into oral and respiratory secretions.

Viremia is accompanied by nonspecific flu-like symptoms.

Bone marrow suppression coincides with viremia.
The illness is biphasic and the second phase coincides with antibody production.

Manifestations are immune-mediated mainly in the form of skin rash, and joint involvement.

Virus is rarely detected in patients with fifth disease because the clinical manifestations are secondary to immune complex formation.

Patients present to medical attention after the period of viremia has passed.
Consistent pathologic changes have been restricted to hematopietic tissue.

Giant pronormoblasts, depletion of later erythroid precursor cells and more occasionally dysplastic changes in myeloid and megakaryocytic cells.

Protective, long-lasting antibody is produced.

Cessation of erythropoiesis lasts 5-7 days.

Cases of ITP and HSP have apparently followed acute parvovirus infection.
Transient Aplastic Crisis

- An abrupt cessation of red blood cell production in the bone marrow in persons with underlying hemolysis.

- It is characterized by reticulocytopenia, absent erythroid precursors in marrow, and precipitous worsening of anemia.

- Transient aplastic crisis results when failed erythropoiesis is combined with a much shortened red blood cell life span.

- Although the illness is self-limited, the patient is acutely ill.
Symptoms may include dyspnea, fatigue, extreme lassitude, confusion, and congestive heart failure.

The crisis can precipitate cerebrovascular accidents in patients with sickle cell disease.

Death can occur from profound anemia and heart failure.

The anemia of TAC is readily treated by blood transfusion. It is rarely complicated by bone marrow necrosis.
TAC occurs in:

- Sickle cell disease
- Congenital erythrocyte membrane defects
- Enzymopathies
- Thalassemia
- Acquired hemolytic anemia in adults.
- Conditions of erythroid stress:
  - hemorrhage and iron deficiency
  - myelofibrosis
  - after bone marrow transplantation.

- It may be followed by pancytopenia with hemophagocytosis.

- TAC is often associated with variable degrees of neutropenia and thrombocytopenia.
Persistent infection

- Pure red cell aplasia.
- Failure to mount a neutralizing antibody response to the virus
- No immune complex mediated symptoms of fifth disease; fever, rash, and polyarthralgia/polyarthritis.
Documented in four patient populations:

- Congenital immunodeficiency (Nezelof’s Syndrome)
- Children with lymphoblastic leukemia and other malignancies in remission after or during chemotherapy
- Patients with AIDS
- Recipients of solid organ transplants.
Clinically, the anemia is severe, and the patient becomes dependent on transfusions.

There may be intermittent neutropenia.

The bone marrow contains giant pronormoblasts.

The anemia may be intermittent, with periods of relapse and remission.
Diagnosis

- **Virus Isolation**
  - Human erythroid progenitors remain the most convenient productive tissue culture system.
  - Bone marrow, peripheral blood, fetal liver, and a few leukemic cells or cell lines have been used to reproduce virus.

- **Serology**
  - IgM and IgG.

- **PCR**
  - most specific