

Parvovirus B19: ...an opportunist.

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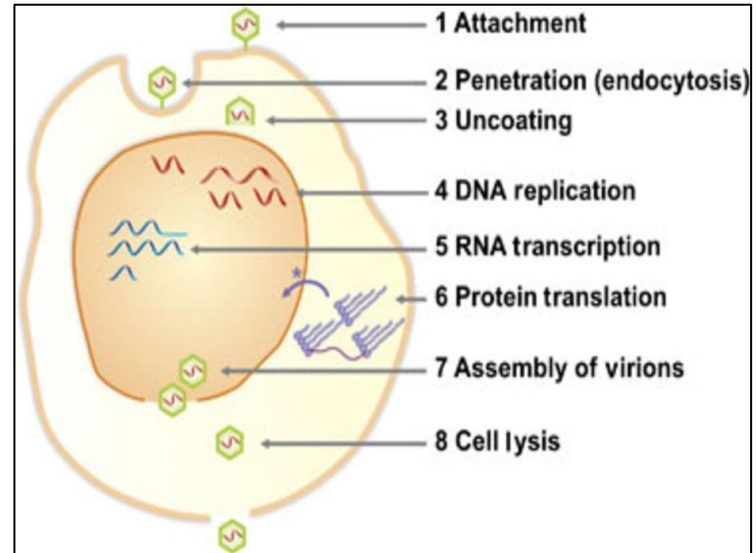
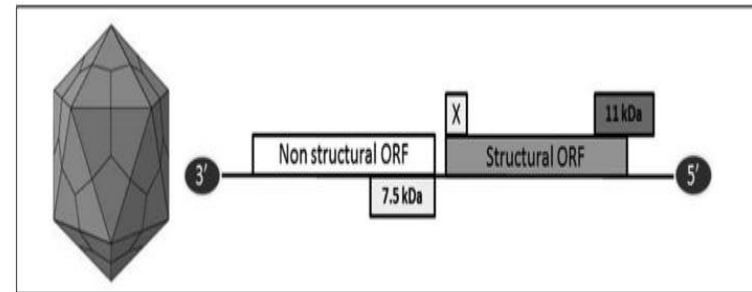
NHLS / WITS



Parvovirus B19:

Virology:

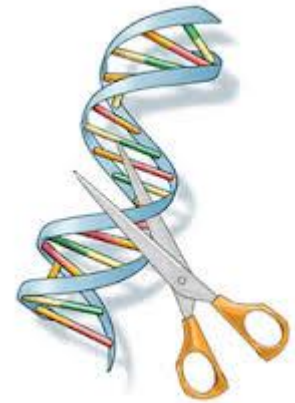
- Discovered in 1975
- Single-stranded, protein encapsulated DNA virus
 - 5 596 nucleotides = small
 - 4 830: coding sequence
 - 2 structural proteins (VP1 & 2): = capsid
 - Non-structural protein (NS1): = replication
 - 383: terminal repeats in hairpin loops
- Replication
 - requires host cell DNA machinery
 - primarily in erythroblasts
- 3 distinct genotypes with variable clinical manifestations
- Persists lifelong in various tissues



Parvovirus B19:

Virology:

- Parvovirus non-structural protein (NS1):
 - localises to nucleus of infected cells
 - cytotoxic to host cells
 - DNA nickase activity
 - Up-regulates expression of pro-inflammatory cytokines:
 - Interleukin 6 (IL-6)
 - Tumour necrosis factor α
 - induce apoptosis in erythroid cells



Parvovirus B19:

Virology:

- Cellular receptor: the glycosphingolipid blood group P antigen (Globoside 4 (Gb4)):
 - Widespread expression:
 - erythrocytes, platelets, granulocytes, lung, heart, synovium, liver, kidney, endothelium, placenta, foetal cells and vascular smooth muscle....

Parvovirus B19:

Clinical manifestations

- Commonly causes:
 - Erythema infectiosum (Fifth disease)
 - Arthralgia
 - Foetal death (Hydrops foetalis)
 - Transient aplastic crisis
 - if RBC survival is shortened in
e.g. Sickle cell disease
 - **Persistent infection in immunocompromised**
- Less common manifestations
 - Neurological syndromes
 - Cardiac syndromes
 - Cytopenias (bone marrow infection)
 - Autoimmune diseases

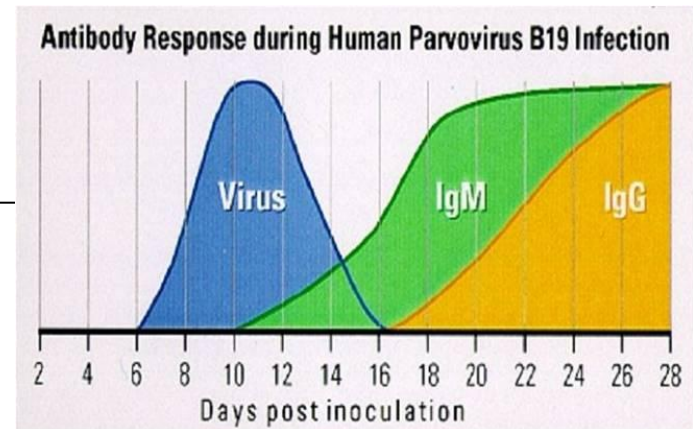


Parvovirus B19:

Epidemiology and transmission

- Transmission:
 - Respiratory aerosol spread from acutely infected
 - multiplies in throat → viraemia on day 6 → infection of erythroblasts in bone marrow
 - Mother-to-child
 - Blood products (heat and solvent resistant)
- Massive productive replication in erythroid progenitor cells
 - very high viral load in acute infection prior to a detectable immune response
 - Up to 10^{13} viral particles per ml of peripheral blood
- Occurs worldwide but restricted to humans
 - Seroprevalence increases with age
 - Up to 90% of adults

Parvovirus B19: Immune response

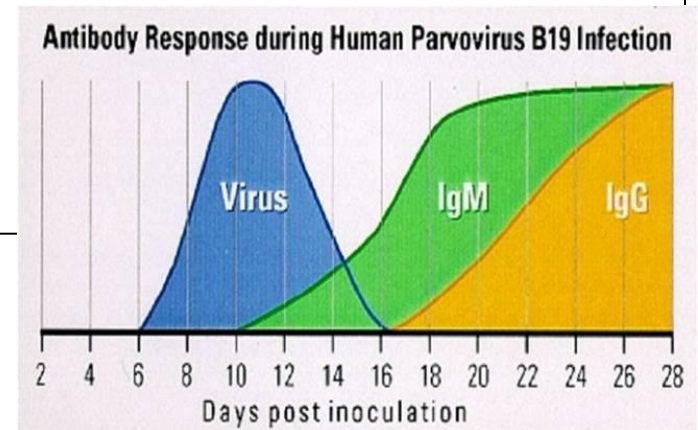


- In immune competent:
 - Virus capsid-specific IgM / IgG Abs produced:
 - Resolution of infection and neutralisation of virus
 - Lymphoproliferative responses:
 - Probably important in long-term control of the virus

Parvovirus B19: Immune response

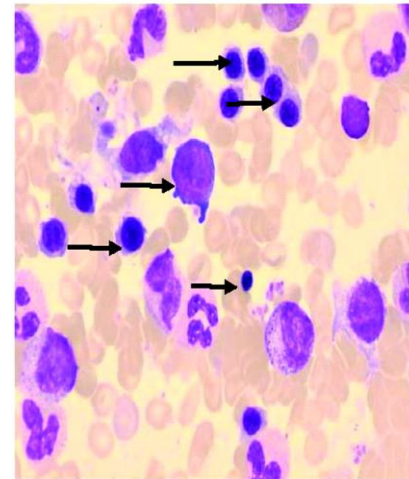
In immune compromised e.g. HIV:

- New Parvo infection or reactivation
- Unable to produce neutralising antibodies → chronic infection with erythroblast lysis → chronic anaemia (pure red cell aplasia (PRCA))
- Anti-retroviral therapy (ART) with immune reconstitution →
 - decreased prevalence of Parvovirus associated PRCA
 - If infected: benign Fifth disease
- Dissociation between serological and molecular PCR results in HIV infected patients
 - inability of the immunocompromised to produce neutralising antibodies
 - immune response may be quantitatively and qualitatively altered
 - diagnostic genome detection on PCR is advocated

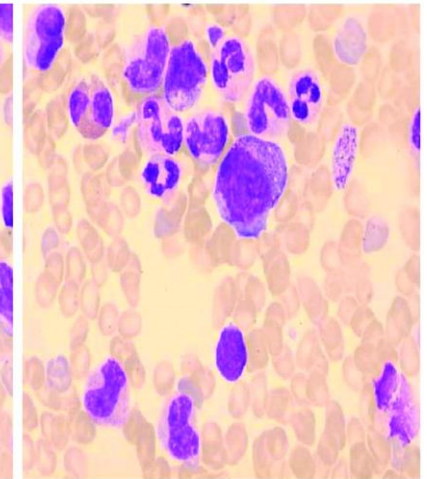


Pure red cell aplasia:

- Absence of maturing erythroid precursors in otherwise normocellular bone marrow
- Causes:
 - Idiopathic
 - Congenital
 - Acquired
 - Lymphoproliferative disorders
 - Neoplastic disorders e.g. Thymoma
 - Autoimmune diseases e.g. Systemic lupus erythematosus (SLE)
 - Pregnancy
 - Recombinant human erythropoietin
 - ABO-incompatible hematopoietic stem cell transplant
 - Myelodysplasia
 - **Chronic parvovirus B19 infection**



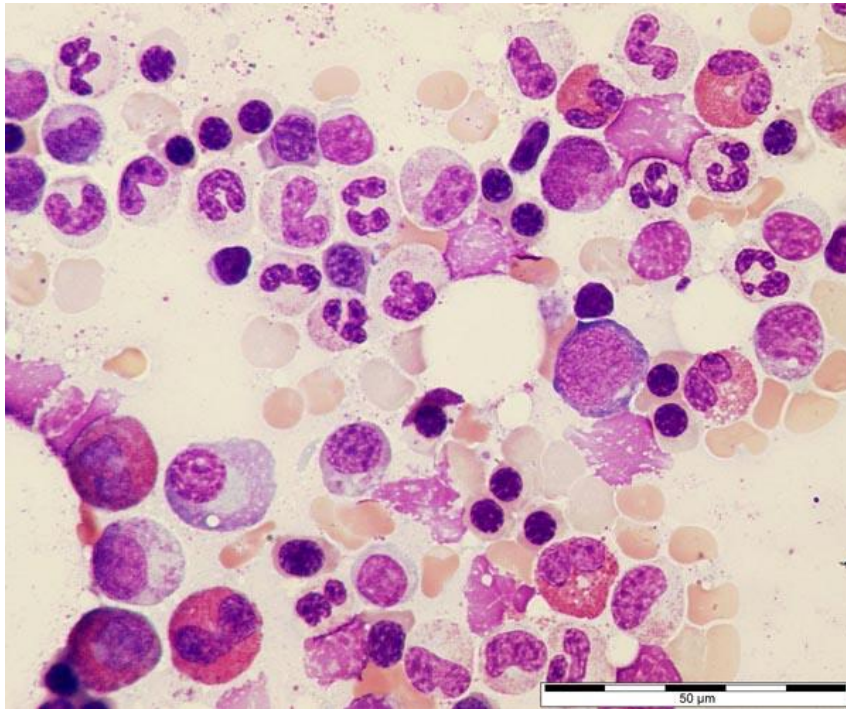
Normal BM containing polychromatophilic erythroblasts (arrows)



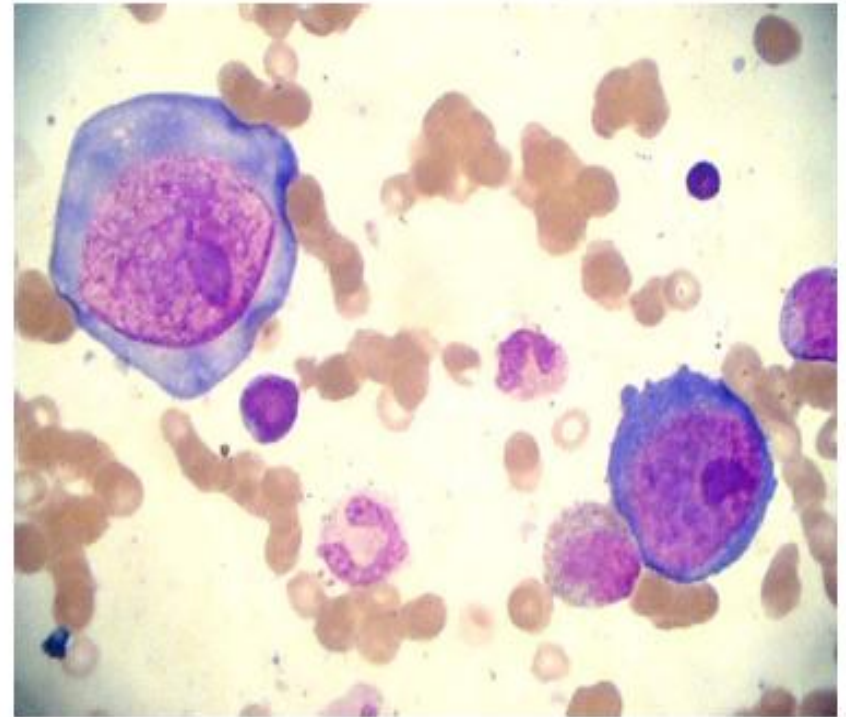
BM of a patient with Ab-mediated PRCA

Parvovirus B19: Pure Red Cell Aplasia (PRCA):

Normal erythropoiesis:



Parvovirus related PRCA:



Parvovirus B19 PRCA: Diagnosis:

- Clinical and routine blood tests
 - FBC Diff, RPI, haematinics etc.
- Serology
 - ELISA: IgG and IgM: **Unreliable in HIV**
- Polymerase chain reaction (PCR)
 - Sensitive
 - Contamination can occur
 - DNA detection in serum and various tissue samples
 - +ve extended periods: low levels of B19 DNA alone: NOT diagnose acute or ongoing infection: **clinical interpretation**
 - most primer pairs based detects geographically diverse B19 isolates BUT many primer pairs would not detect the V9 variant
 - Ideally 2 sets of primers should be used



Parvovirus B19 PRCA: Treatment

- Supportive blood transfusions at ~R1 684 per unit
 - Iron overload and blood scarcity
- Polygam (iVIG)
 - Example of a regimen:
 - Dose: ± 3 doses (1.3 ± 0.5 g/kg/dose)
 - BUT HB can correct with 1 dose
 - Haemoglobin improved after 80 ± 54 days
 - Side-effects: acute reversible renal failure and pulmonary oedema
 - 33.9% relapse rate at a mean of 4.3 months
 - ~ R 40 000 per course
- Anti-retroviral therapy (ART) with immune reconstitution

TEKA WAY

SD-HALAL



TEKAWAY
SUSHI



Teka Away message:

- Parvovirus co-infection in people living with HIV contributes to:
 - Morbidity
 - Mortality
 - Decreased quality of life
 - Add to cost of treatment and investigations
- Paucity of research and publications from SA....