Parvovirus B19: ...an opportunist.

Dr Susan Louw
Haematopathologist
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
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 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....