

# The Immunomodulatory Role of IVIg in Viral Induced Neuro-immune Disorders

## The Potential Role of Anti-myelin Antibodies as a Biomarker

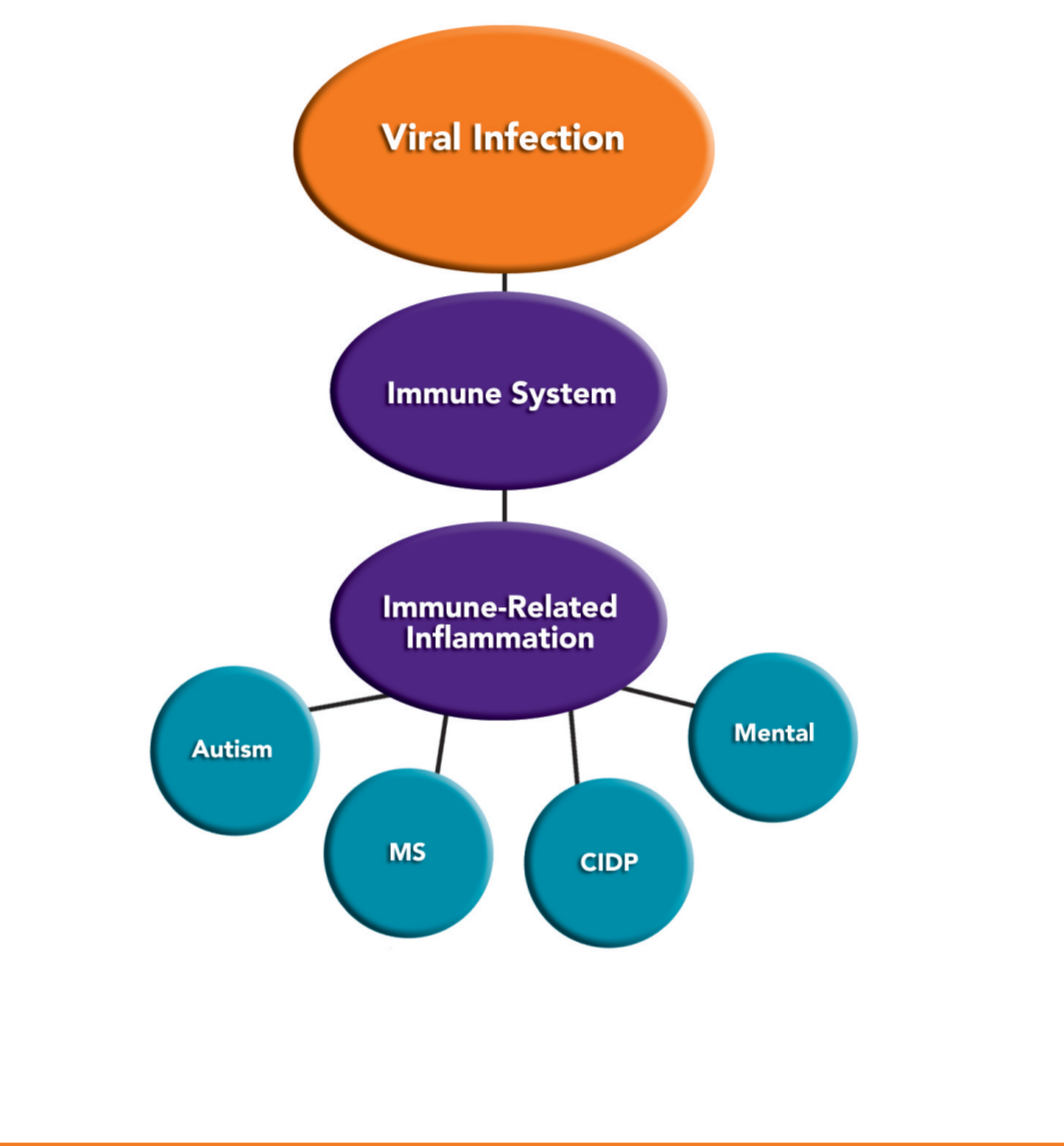


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### AIMS HYPOTHESIS FAILURE OF APOPTOSIS CAUSE OF PERSISTENT INFLAMMATION RESULTS

- To understand the role of viral pathogens, specifically parvovirus B19 (B19) in the etiology of neuro-immune disorders
- To evaluate the immunomodulatory effect of IVIg on viral induced neuro-immune disease
- To evaluate a potential biomarker for efficacy of immunomodulatory therapy

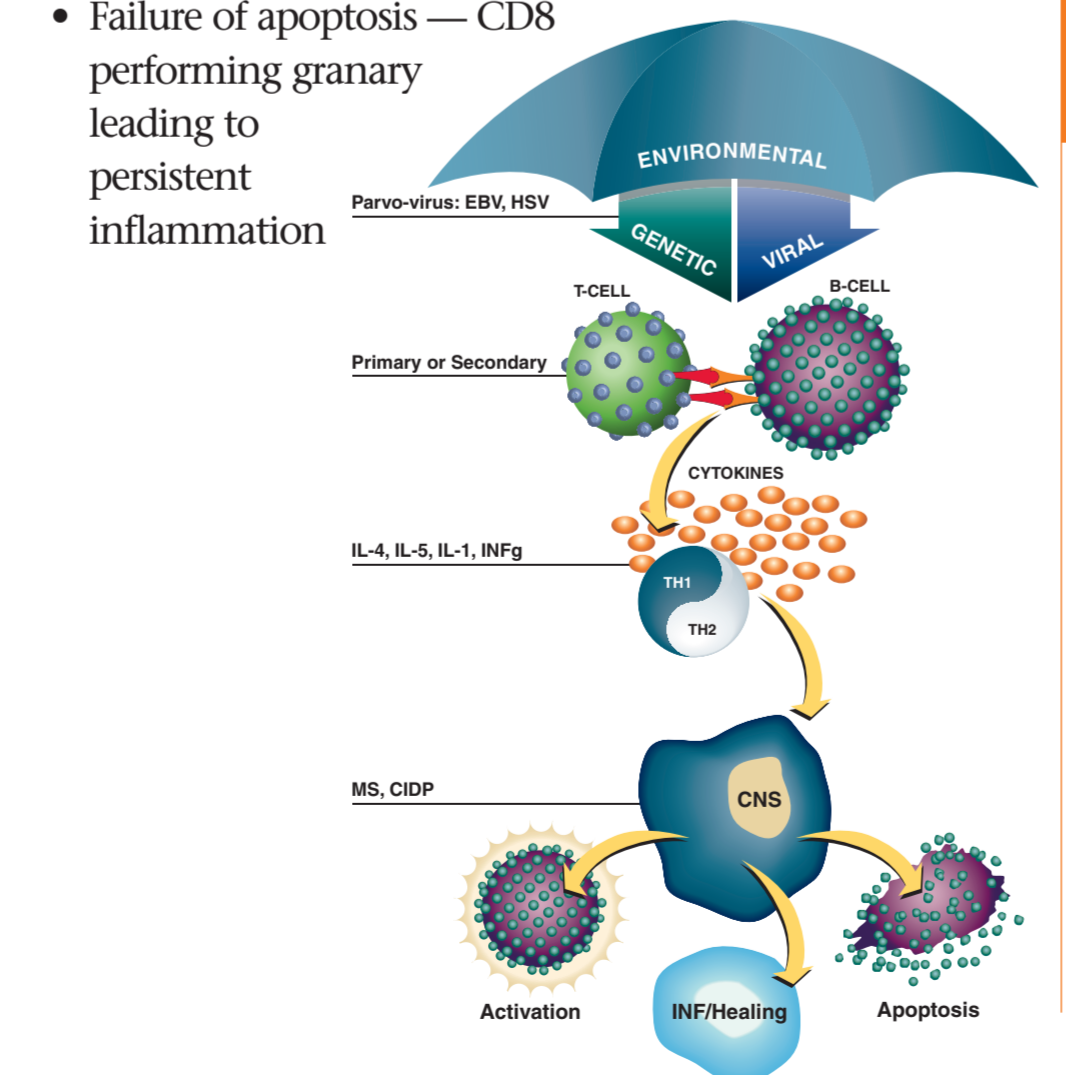
- The interaction of an infectious pathogen like B19 with the immune system can happen via various mechanisms:
- T-cell Receptor (TCR) cross-reactivity with a viral pathogen
  - Molecular mimicry, whereby an infectious pathogen, such as B19, can initiate a response in which a T- or B-cell component cross-recognizes and leads to cross-reaction with the myelin
  - Super-antigens: viral antigens initiate an immediate T-cell response, activating different signaling pathways leading to an abnormal neuro-immune response
  - Viral infections can trigger autoimmune T-cell reactions either by molecular mimicking or by bystander activation
  - Furthermore, viral infection or an infectious context may contribute to skewing an immune response toward a proinflammatory phenotype by activation of Toll-like receptors and the cytokines IL-1, IL-6 and TNF
  - Failure of the specific viral immunity to eliminate the virus or to eliminate the by-products induced by the virus
  - Failure of apoptosis — CD8 performing granary leading to persistent inflammation



- All patients displayed major improvement in clinical outcomes
- Decreased levels of B19
- AMA levels correlated with clinical outcomes and B19 levels

### INTRODUCTION

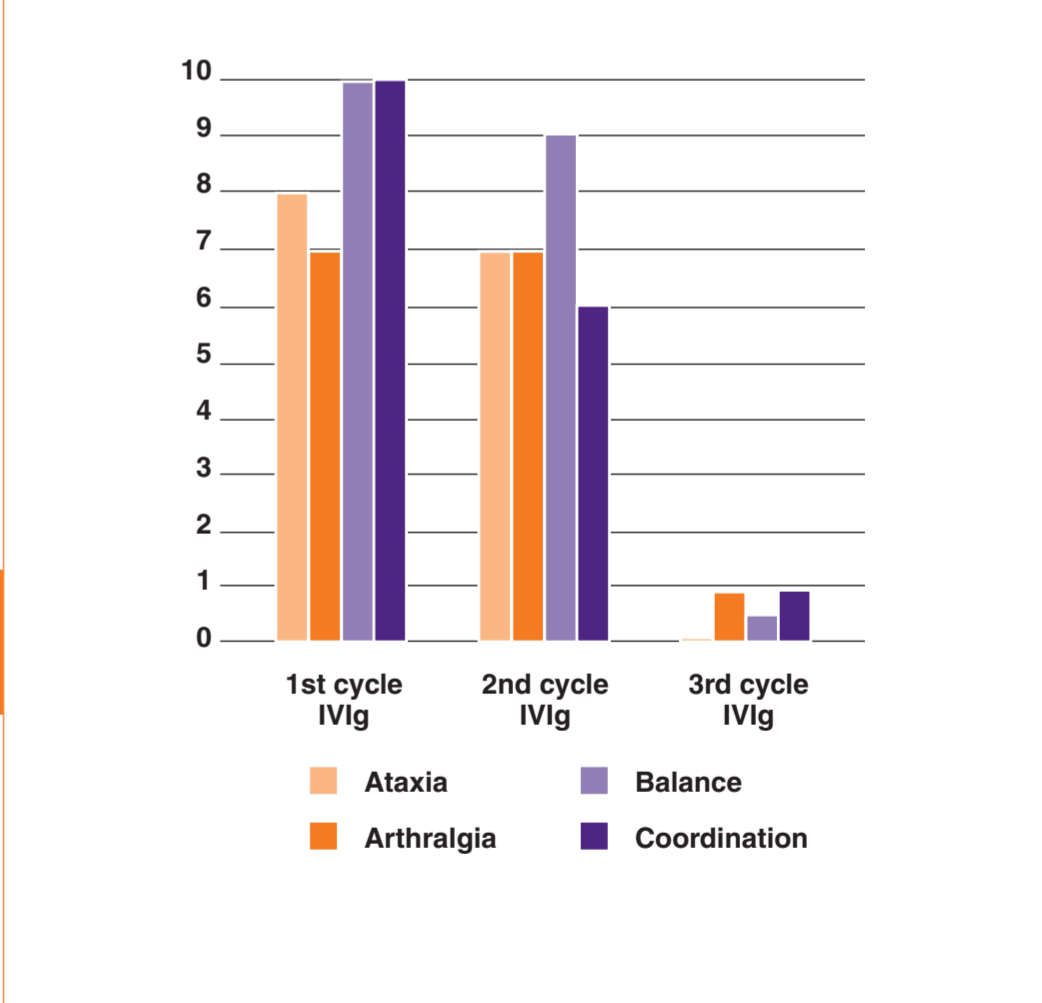
- Many patients present with ataxia and nonspecific signs and symptoms of neurological disease such as: fatigue, lack of coordination and balance, and muscle weakness
- We and others have observed that a subset of patients with high titers of B19 IgG or IgM experience these neurological symptoms
- B19 is a non-enveloped, single-stranded DNA virus that contains two structural proteins, VP1 and VP2
- The VP1 region has been shown to induce the production of pro-inflammatory cytokines, e.g., TNF alpha and IL-6
- Preliminary in vitro investigation demonstrates cross reactivity of B19 IgG with myelin basic protein providing a plausible relationship between positive B19 serology and a demyelinating syndrome of unknown origin
- This implicates a possible role for B19 IgG in the pathogenesis of a demyelinating syndrome
- Anti-myelin antibodies (AMA) are indicative of neuroinflammation
- AMA, in our experience, has correlated to therapeutic efficacy in modulating this inflammation



### SUMMARIZED DESCRIPTION OF THE METHODOLOGY

- In this study, we present 10 patients:
- Diagnosed with immune deficiency
  - Positive IgG and IgM antibodies to B19
  - Elevated levels of AMA
  - Neuro-immune presentation: ataxia, tremor, MS-like symptoms, progressive dyspraxia and neuropathy
  - All patients received high-dose of IVIg between 1 – 2 g/kg body weight
  - Endpoints for therapy were:
    - Clinical evaluations
    - Laboratory levels including AMA
    - B19 levels

**The Linkage Between Viral Infections to Auto Immune — Neurological Disease**  
 (Ranking symptoms on a scale of 1 – 10, with least affected ranked a 1 and most severely affected ranked a 10)



### CONCLUSIONS

- B19 can effect CNS by causing neuroinflammation
- High-dose IVIg can re-modulate the neurological manifestation associated with B19 and down-regulate B19 IgM response
- AMA may be a biomarker to determine efficacy of treatment to reduce neuroinflammation