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Abstract

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Immunological findings in autism.

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Abstract

The immunopathogenesis of **autism** is presented schematically in Fig. 1. Two main immune dysfunctions in **autism** are immune regulation involving pro-inflammatory cytokines and autoimmunity. Mercury and an infectious agent like the measles virus are currently two main candidate environmental triggers for immune dysfunction in **autism**. Genetically immune dysfunction in **autism** involves the MHC region, as this is an immunologic gene cluster whose gene products are Class I, II, and III molecules. Class I and II molecules are associated with antigen presentation. The antigen in virus infection initiated by the virus particle itself while the cytokine production and inflammatory mediators are due to the response to the putative antigen in question. The cell-mediated immunity is impaired as evidenced by low numbers of CD4 cells and a concomitant T-cell polarity with an imbalance of Th1/Th2 subsets toward Th2. Impaired humoral immunity on the other hand is evidenced by decreased IgA causing poor gut protection. Studies showing elevated brain specific antibodies in **autism** support an autoimmune mechanism. Viruses may initiate the process but the subsequent activation of cytokines is the damaging factor associated with **autism**. Virus specific antibodies associated with measles virus have been demonstrated in **autistic** subjects. Environmental exposure to mercury is believed to harm human health possibly through modulation of immune homeostasis. A mercury link with the immune system has been postulated due to the involvement of postnatal exposure to thimerosal, a preservative added in the MMR vaccines. The occupational hazard exposure to mercury causes edema in astrocytes and, at the molecular level, the CD95/Fas apoptotic signaling pathway is disrupted by Hg^{2+}. Inflammatory mediators in **autism** usually involve activation of astrocytes and microglial cells. Proinflammatory chemokines (MCP-1 and TARC), and an anti-inflammatory and modulatory cytokine, TGF-beta1, are consistently elevated in **autistic** brains. In measles virus infection, it has been postulated that there is immune suppression by inhibiting T-cell proliferation and maturation and downregulation MHC class II expression. Cytokine alteration of TNF-alpha is increased in **autistic** populations. Toll-like-receptors are also involved in **autistic** development. High NO levels are associated with **autism**. Maternal antibodies may trigger **autism** as a

mechanism of autoimmunity. MMR vaccination may increase risk for **autism** via an autoimmune mechanism in **autism**. MMR antibodies are significantly higher in **autistic** children as compared to normal children, supporting a role of MMR in **autism**. Autoantibodies (IgG isotype) to neuron-axon filament protein (NAFP) and glial fibrillary acidic protein (GFAP) are significantly increased in **autistic** patients (Singh et al., 1997). Increase in Th2 may explain the increased autoimmunity, such as the findings of antibodies to MBP and neuronal axonal filaments in the brain. There is further evidence that there are other participants in the autoimmune phenomenon. (Kozlovskaia et al., 2000). The possibility of its involvement in **autism** cannot be ruled out. Further investigations at immunological, cellular, molecular, and genetic levels will allow researchers to continue to unravel the immunopathogenic mechanisms' associated with **autistic** processes in the developing brain. This may open up new avenues for prevention and/or cure of this devastating neurodevelopmental **disorder**.

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