

# Chronic Fatigue Syndrome & **IVIG**

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Am J Med. 1990 Nov;89(5):561-8.

## **A double-blind, placebo-controlled trial of intravenous immunoglobulin therapy in patients with chronic fatigue syndrome.**

**Lloyd A, Hickie I, Wakefield D, Boughton C, Dwyer J.**

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**PURPOSE:** The chronic fatigue syndrome (CFS) is characterized by profound fatigue, neuropsychiatric dysfunction, and frequent abnormalities in cell-mediated immunity. No effective therapy is known. **PATIENTS AND METHODS:** Forty-nine patients (40 with abnormal cell-mediated immunity) participated in a randomized, double-blind, placebo-controlled trial to determine the effectiveness of high-dose intravenously administered immunoglobulin G. The patients received three intravenous infusions of a placebo solution or immunoglobulin at a dose of 2 g/kg/month. Assessment of the severity of symptoms and associated disability, both before and after treatment, was completed at detailed interviews by a physician and psychiatrist, who were unaware of the treatment status. In addition, any change in physical symptoms and functional capacity was recorded using visual analogue scales, while changes in psychologic morbidity were assessed using patient-rated indices of depression. Cell-mediated immunity was evaluated by T-cell subset analysis, delayed-type hypersensitivity skin testing, and lymphocyte transformation with phytohemagglutinin. **RESULTS:** At the interview conducted by the physician 3 months after the final infusion, 10 of 23 (43%) immunoglobulin recipients and three of the 26 (12%) placebo recipients were assessed as having responded with a substantial reduction in their symptoms and recommencement of work, leisure, and social activities. The patients designated as having responded had improvement in physical, psychologic, and immunologic measures (p less than 0.01 for each). **CONCLUSION:** Immunomodulatory treatment with immunoglobulin is effective in a significant number of patients with CFS, a finding that supports the concept that an immunologic disturbance may be important in the pathogenesis of this disorder.

PMID: 2146875 [PubMed - indexed for MEDLINE]  
: J Psychiatr Res. 1997 Jan-Feb;31(1):133-47.

## **Double-blind randomized controlled trial to assess the efficacy of intravenous gammaglobulin for the management of chronic fatigue syndrome in adolescents.**

**Rowe KS.**

Department of Paediatrics, University of Melbourne Royal Children's Hospital, Victoria, Australia.

A double blind randomized controlled trial was conducted in 71 adolescents aged 11-18 years. Inclusion in the trial required fulfilment of the diagnostic criteria, (Fukuda et al., 1994). Three infusions of 1 gm/kg (max 1 litre of 6 gm/100 ml in 10% w/v maltose solution) were given one month apart. The dummy solution was a 10% w/v maltose solution with 1% albumin of equivalent volume for weight. Efficacy was assessed by difference in a mean functional score including school attendance, school work, social activity and physical activity, between baseline, three months and six months after the final infusion. There was a significant mean functional improvement at the six month follow-up of 70 adolescents with Chronic Fatigue Syndrome of average duration 18 months.

Med J Aust. 1989 Aug 7;151(3):122-4.

### **Immunological abnormalities in the chronic fatigue syndrome.**

**Lloyd AR, Wakefield D, Boughton CR, Dwyer JM.**

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The chronic fatigue syndrome is a disorder of unknown aetiology which is characterized by debilitating fatigue. Recent evidence has suggested that viruses may persist in the tissues of patients with chronic fatigue syndrome. A concurrent immunological disturbance is likely to be associated with the persistence of viral antigens. Therefore, the humoral and cellular immunity of 100 patients who were suffering from chronic fatigue syndrome and that of 100 healthy, age- and sex-matched control subjects were compared. This study documents the frequent occurrence of abnormalities within the cellular and humoral immune systems of patients with well-defined chronic fatigue syndrome. Disordered immunity may be central to the pathogenesis of chronic fatigue syndrome. In patients with chronic fatigue syndrome, a significant (P less than 0.01) reduction was found in the absolute number of peripheral blood lymphocytes in the total T-cell (CD2), the helper/inducer T-cell (CD4) and the suppressor/cytotoxic T-cell (CD8) subsets. A significant (P less than 0.001) reduction also was found in T-cell function, which was measured: in vivo by delayed-type hypersensitivity skin-testing (reduced responses were recorded in 50 [88%] of 57 patients); and in vitro by phytohaemagglutinin stimulation. Reduced immunoglobulin (Ig) levels were common (56% of patients), with the levels of serum IgG3- and IgG1-subclasses particularly (P less than 0.05) affected.

PMID: 2787888 [PubMed - indexed for MEDLINE]

Curr Pain Headache Rep. 2003 Oct;7(5):333-41.

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**Cytokines in parvovirus B19 infection as an aid to understanding**

## **chronic fatigue syndrome.**

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Human parvovirus B19 infection has been associated with various clinical manifestations of a rheumatic nature such as arthritis, fatigue, and chronic fatigue syndrome (CFS), which can persist for years after the acute phase. The authors have demonstrated recently that acute B19 infection is accompanied by raised circulating levels of IL-1b, IL-6, TNF-a, and IFN-g and that raised circulating levels of TNF-a and IFN-g persist and are accompanied by MCP-1 in those patients who develop CFS. A resolution of clinical symptoms and cytokine dysregulation after intravenous immunoglobulin (IVIG) therapy, which is the only specific treatment for parvovirus B19 infection, also has been reported. Although CFS may be caused by various microbial and other triggers, that triggered by B19 virus is clinically indistinguishable from idiopathic CFS and exhibits similar cytokine abnormalities and may represent an accessible model for the study of CFS.

Publication Types:

PMID: 12946285 [PubMed - indexed for MEDLINE]

Clin Infect Dis. 2003 May 1;36(9):e100-6. Epub 2003 Apr 22.

### **Successful intravenous immunoglobulin therapy in 3 cases of parvovirus B19-associated chronic fatigue syndrome.**

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Three cases of chronic fatigue syndrome (CFS) that followed acute parvovirus B19 infection were treated with a 5-day course of intravenous immunoglobulin (IVIG; 400 mg/kg per day), the only specific treatment for parvovirus B19 infection. We examined the influence of IVIG treatment on the production of cytokines and chemokines in individuals with CFS due to parvovirus B19. IVIG therapy led to clearance of parvovirus B19 viremia, resolution of symptoms, and improvement in physical and functional ability in all patients, as well as resolution of cytokine dysregulation.

PMID: 12715326 [PubMed - indexed for MEDLINE]

Postepy Hig Med Dosw. 2002;56 Suppl:91-102.

## [Use of IVIG in secondary immunodeficiencies]

**Zeman K, Lewandowicz-Uszynska A.**

Zaklad Immunologii Klinicznej Instytutu Centrum Zdrowia Matki Polki i Zaklad Immunologii Klinicznej WAM w lodzi. zeman@achilles.wam.lodz.pl

The research connects usefulness of intravenous preparates of immunoglobulins in patients with secondary immunodeficiencies. Basing on the data of literature there was discussed the using IVIG in patients with HIV infection and with the chronic fatigue syndrome. There was also discussed the matt of using IVIG after multiorgans traumas, burns and operations with high risk complications.

PMID: 12661419 [PubMed - indexed for MEDLINE]

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Scand J Immunol. 1991 Mar;33(3):319-27.

### **A comprehensive immunological analysis in chronic fatigue syndrome.**

**Gupta S, Vayuvegula B.**

Division of Basic and Clinical Immunology, University of California, Irvine 92717.

A detailed analysis of cell-mediated and antibody-mediated immunity was performed in 20 CDC-defined patients with chronic fatigue syndrome (CFS) and 20 age- and sex-matched healthy controls. CD3+, CD4+, CD8+, and CD20+ lymphocytes were comparable in two groups. Natural killer cells as defined by CD16, CD56 and CD57 antigens were significantly reduced in CFS. A significant increase in the proportions of CD4+ ICAM 1+ T cells was observed in CFS. Monocytes from CFS displayed increased density (as determined by mean fluorescence channel numbers) of intercellular adhesion molecule 1 (ICAM-1) and lymphocyte function associated antigen 1 (LFA-1), but showed decreased enhancing response to recombinant interferon-gamma in vitro. The lymphocyte DNA synthesis in response to phytohaemoglobin (PHA), Concanavalin A (Con A) and pokeweed mitogen (PWM) was normal but the response to soluble antigens was significantly reduced. Serum IgM, IgG, IgA, and IgG subclasses were normal. In vivo specific antibody response to pneumococcus vaccine was depressed in CFS. Forty percent of patients showed titres of anti-human herpes virus 6 (anti-HHV-6) antibody higher than that in the controls (greater than or equal to 1/80). These data suggest immunological dysfunction in patients with chronic fatigue syndrome. The significance of these observations is discussed.

PMID: 1849315 [PubMed - indexed for MEDLINE]

Clin Infect Dis. 1994 Jan;18 Suppl 1:S136-41.

[Related Articles, Links](#)

## **Immunologic abnormalities associated with chronic fatigue syndrome.**

**Barker E, Fujimura SF, Fadem MB, Landay AL, Levy JA.**

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Several aspects of cellular immunity in patients with clinically defined chronic fatigue syndrome (CFS) were evaluated and compared with those in healthy individuals. Flow cytometric analyses revealed normal expression of total T (CD3+), B (CD19+), and NK (natural killer) (CD16+, CD56+) markers on the surface of peripheral blood mononuclear cells (PMC) from patients with CFS. However, compared with those of healthy individuals, patients' CD8+ T cells expressed reduced levels of CD11b and expressed the activation markers CD38 and HLA-DR at elevated levels. In many of the individuals in whom expression of CD11b was reduced the expression of CD28 was increased. These findings indicate expansion of a population of activated CD8+ cytotoxic T lymphocytes. A marked decrease in NK cell activity was found in almost all patients with CFS, as compared with that in healthy individuals. No substantial abnormalities in monocyte activity or T cell proliferation were observed. The results of this study suggest that immune cell phenotype changes and NK cell dysfunction are common manifestations of CFS.

PMID: 8148441 [PubMed - indexed for MEDLINE]

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