imran700usa@yahoo.com www.cidpusa.org

The cause of Epilepsys is difficult to diagnose and it is challenging to control the seizures with drugs. Crescent Healthcare presents a series articles which show that IVIG is effective in controlling epilepsy and show that some cases of epilepsy are caused by immune disease. Imran Khan

Med Pregl. 1992;45(5-6):220-4.

[Malignant epilepsy in children: therapy with high doses of intravenous immunoglobulin]
Sterio M, Gebauer E, Felle D, Vucicevic G, Zalisevskij G.

22 children with intractable childhood epilepsy (ICE) showing no response to conventional drugs of hormone (ACTH, Synacten) therapy were administered i.v. immunoglobulin (ENDOBULIN immuno) at a dosage of 400 mg/kg on the first and 15th day and subsequently every 3 weeks for 6 months. 12/22 patients showed IgG2 subclass deficiency. A significant reduction in attacks, or even absence of attacks was observed in 13/22 children after 6 months of i.v. immunoglobulin therapy. Most of this children showed IgG2 subclass deficiency. The reduction of attacks after i.v. immunoglobulin therapy correlated with the improvement or normalization of the EEG finding. As for the psychomotor development, no major changes were noticed with respect to the condition prior to the therapy, but in children with IgG2 deficiency, there is no further psychomotor deterioration. 6 months after the last i.v. immunoglobulin dose positive therapeutic effect remained in 5/22 children, with 3 children the therapy was repeated because of recidive attacks and worse EEG findings, and proved effective. Light worsening of the EEG findings was found in 3/22 children, 2/22 dropped out, 1/22 child died of intercurrent infection, and in girl the attacks ceased entirely 4 months after the last i.v. immunoglobulin dose. With other children the condition remained unchanged. According to the authors opinion, i.v. immunoglobulin has its own place in ICE treatment, and it is evident in all cases where the classical antiepileptic and/or hormone therapy was unsuccessful, especially in children with IgG2 subclass deficiency, that is, in all the epilepsy cases where a great number of attacks is imperilling the psychomotor development in children, independently of type.

Wien Klin Wochenschr. 1990 Apr 13;102(8):230-3.

[Intravenous immunoglobulin in the treatment of malignant epilepsy in children]
Sterio M, Gebauer E, Vucicevic G, Zalisevskij G, Felle D, Kolarov N.

15 children with malignant epilepsy showing no response to conventional antiepileptic drugs or hormone therapy were administered intravenous immunoglobulin (Endobulin, Immuno) at a dosage of 400 mg/kg per day on the 1st and 15th day and subsequently every three weeks for 6 months. 7 of these 15 patients showed IgG2 subclass deficiency. A significant reduction in attacks, or even absence of attacks was observed in 10 out of 15 children after six months of intravenous immunoglobulin therapy. Apart from one patient with ringchromosomopathy, all the children with IgG2 subclass deficiency responded to this therapy. The reduction of attacks after i.v. immunoglobulin therapy correlates with the improvement or normalization of the EEG findings. At present, the authors consider the number of patients still too small to make a final assessment, but they believe that intravenous immunoglobulin holds an important position in the treatment of malignant epilepsy in childhood.

Monogr Allergy. 1986;20:128-34.

IgG2 deficiency and intractable epilepsy of childhood.
Duse M, Tiberti S, Plebani A, Avanzini MA, Gardenghi M, Menegati E, Monafo V, Ugazio AG.

Twelve children with intractable childhood epilepsy (ICE) were treated with high-dose intravenous immunoglobulins every 21 days for 6 months after immunologic and neurologic evaluations had been carried out. 50% (6/12) were found to have a deficiency of serum IgG2 and all but 1 of these responded to treatment with marked reduction in the daily number of seizures assessed both clinically and electroencephalographically. The response to treatment was, in fact, significantly higher in the children with IgG2 deficiency than in the others. IgG4 deficiency, observed in 5 children, did not affect treatment response. It is suggested that IgG2 deficiency may predispose to some form of viral encephalitis which may trigger an immune mechanism leading to the ICE.

Acta Neurol Scand. 1993 Sep;88(3):204-9.

Intravenous high-dose gammaglobulins for intractable childhood epilepsy.
Gross-Tsur V, Shalev RS, Kazir E, Engelhard D, Amir N.
Florence Miller EEG Diagnostic Unit, Neuropediatric Unit Shaare Zedek Medical Center, Jerusalem, Israel.

Immunological mechanisms have been implicated in the pathogenesis of epileptic seizures in some patients and in experimental animal models of epilepsy. A beneficial effect of high dose intravenous gammaglobulin (IVIG) has been demonstrated for some children with intractable epilepsy. In this study we treated 9 children ages 1.1-9.2 years (mean 5.0 years) with intractable epilepsy not responsive to conventional antiepileptic drugs (AEDs) and steroid therapy. Eight children had Lennox-Gastaut syndrome and 1 had complex partial seizures with secondary generalization. Each child received 3 doses of IVIG (200 mg/kg of polyvalent immunoglobulin) on Days 1, 15 and 36. Concomitant AEDs were not changed. Four children had complete remission, 3 had partial response with a more than 50% reduction in seizure frequency and 2 had no response. Onset of response varied from immediate to 7 months after the last injection. No toxicity was noted. Duration of remission was 9 months in 1 case. The other 3 cases have remained in remission to date with a follow up period of 22-26 months. We conclude that IVIG is a safe therapy which appears to be effective in some children with intractable seizures. Children with shorter duration of their seizure disorder (< 1 year) and relatively preserved cognitive function (IQ > 70) appear to have a more favorable response. Larger scale controlled trials are needed to determine the optimal timing and dosage, as well as to identify specific subgroups which may benefit most from IVIG treatment.

Eur Arch Psychiatry Neurol Sci. 1986;236(2):119-22.

Treatment of idiopathic West and Lennox-Gastaut syndromes by intravenous administration of human polyvalent immunoglobulins.
van Rijckevorsel-Harmant K, Delire M, Rucquoy-Ponsar M.

A total of 7 patients (3-21 years old) suffering from an intractable "primary" Lennox-Gastaut syndrome (LGS) were treated with i.v. high doses of polyvalent human immunoglobulins. Of these patients 6 improved following such treatment with a decrease in fits and an improvement in the EEG. Hypotheses about the contribution of the treatment and immunopathological factors in some cases of idiopathic LGS are discussed.

Neuropediatrics. 1990 May;21(2):87-90.

Intravenous immunoglobulin: a single-blind trial in children with Lennox-Gastaut syndrome.
Illum N, Taudorf K, Heilmann C, Smith T, Wulff K, Mansa B, Platz P.

The antiepileptic effect of intravenous immunoglobulin (Sandoglobulin, Sandoz) was investigated in Lennox-Gastaut syndrome by an add-on, placebo-controlled, single-blind trial. Ten patients, aged 4-14 years, with insufficient response to conventional anticonvulsive therapy received placebo and Sandoglobulin 400 mg/kg two times each with an interval of two weeks. The washout period was four weeks and the total observation period 14 weeks, during which parents daily registered number and type of seizures. EEG, in vitro lymphocyte transformation tests and concentrations of immunoglobulins including IgG subclasses were evaluated before and after active treatment. Two children showed an immediate reduction in their high-frequency and invariable seizure activity from 42% to 100% and a less abnormal EEG. In addition, general well-being and intellectual performance was improved. The strongest response was observed in one child with a concomitant finding of a low level of IgG2, the only abnormal immunologic test in this study. The remaining 8 children, who had either a high or a low but variable seizure frequency showed no immediate change as EEG and their general condition was unaffected. We conclude that intravenous immunoglobulin had an immediate and pronounced effect on break-through seizure activity and a simultaneous neurophysiologic effect in 20% of our patients with Lennox-Gastaut syndrome. The effect was not confined to patients with immunologic abnormalities.

Acta Paediatr. 1992 Aug;81(8):646-8.

Phenytoin-induced IgG2 and IgG4 deficiencies in a patient with epilepsy.

Ishizaka A, Nakanishi M, Kasahara E, Mizutani K, Sakiyama Y, Matsumoto S.

Department of Pediatrics, Hokkaido University School of Medicine, Sapporo, Japan.

A five-year-old girl with epilepsy and recurrent respiratory infections was investigated for serum IgG subclass concentrations. She was diagnosed as having a combined deficiency of IgG2 and IgG4 with a decreased serum concentration of IgA and IgG3 and was given replacement therapy with i.v. immunoglobulins. Since then, she has been free from respiratory infections. After phenytoin therapy was stopped, IgG subclass deficiency improved. This case describes the further action of phenytoin on the immune system, adding IgG subclass deficiency to the list.

Rev Electroencephalogr Neurophysiol Clin. 1977 Oct-Dec;7(4):443-7.
[The treatment of epileptic encephalopathies with gamma globulin in children (author's transl)]
Pechadre JC, Sauvezie B, Osier C, Gibert J.
Preliminary Results: The authors have treated 10 children presenting with severe epilepsy with repeated large doses of gamma-globulin. They noted a marked improvement in 7 of the children with respect to behaviour and a disappearance of seizures in 8 with comparable EEG improvement. Four children have been able to reduce their conventional anticonvulsant therapy considerably and 2 others havers received no other medication at all for 8 months. The possibility of an immune disturbance in some childhood epilepsies is thus suggested.

Child Neurol. 2003 Jun;18(6):379-82.

Intravenous immunoglobulin as adjunctive therapy for juvenile spasms.

Bingel U, Pinter JD, Sotero de Menezes M, Rho JM.

University of Washington, Children's Hospital and Regional Medical Center, Seattle, USA.

Intravenous immunoglobulin has been reported to be an effective treatment for infantile spasms. Juvenile spasms are electrically and clinically similar to infantile spasms but occur in a later age group. We retrospectively reviewed the charts of five children (aged 4.5-11.5 years) at our institution. Their primary seizure type was juvenile spasms and they were treated with a single inpatient course of intravenous immunoglobulin (400 mg/kg/day intravenously for 5 consecutive days) on an adjunctive basis. Seizure frequency was determined from parental reports. By 3 months after treatment, improvement (a 50-92% reduction in seizure frequency) was noted in four patients; sustained benefit was seen in three patients for up to 12 months. One patient showed no response at 3 and 6 months and had an increase in seizure frequency at 1 year. We conclude that single-course intravenous immunoglobulin can be effective as adjunctive therapy for juvenile spasms and that benefit can persist for many months. However, larger controlled, prospective clinical trials are needed to validate this unconventional treatment modality for specific seizure types such as juvenile spasms.