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Plasmapheresis for neuropathies

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Background

A number of severe progressive neuropathies are based on the autoimmune pathogenesis, which is considered essential in myasthenia gravis, myasthenic Lambert-Eaton syndrome, Guillain-Barre syndrome, IgM-monoclonal demyelinating polyneuropathy, chronic inflammatory demyelinating polyneuropathy, multifocal motor neuropathy, multiple sclerosis, inflammatory myopathies, syndrome of muscular hypertonicity, autoimmune neuromyotonia, paraneoplastic cerebellar degeneration and neuropathy, neuropathies associated with systemic vasculitis and viral infection. In these disorders autoantibodies affect glial cells, myelin, axon, calcium channels, muscles [Dalakas M.C., 1995].

Demyelinating diseases are widespread in the population with an unstoppable trend to "rejuvenation", with rapid incapacitation and uniquely poor prognosis. Demyelination is due to release of control of T-suppressors with the abolition of immune tolerance to myelin basic protein (MBP). Antibodies against MBP stimulate complement which increases the permeability of the blood-brain barrier to components of the immune system. Antibodies to MBP, specifically affecting the oligodendrocytes and myelin, have myelinolitic and myelinotoxic effects. During the incubation of these antibodies with allogenic MBP a pronounced proteolytic effect is revealed [Vostrikova I.L. et al., 2006].

Currently, the most common viral etiology of the concept of demyelinating diseases, which is the data confirming the presence of common antigenic determinants between the encephalitogenic region of MBP, and several viruses (measles, rubella, Epstein-Barr virus, cytomegalovirus, herpes simplex). Obviously, as a result of a viral infection there is the initial startup of autoimmune disorders, leading to failure of tolerance to MBP and development of severe demyelinating disease. An important role in the pathogenesis of autoimmune diseases is played by cytokines, in particular TNF-α, which strengthen the adhesion of T-lymphocytes ($CD4^+$), macrophage activation, cytolysis oligodendrocytes, and thereby promoting demyelination [Körner H. et al., 1997].

In multiple sclerosis, encephalomyelitis, neuromyelitis optica we can observe accumulation of some unidentifiable substances autoimmune or allergic nature, causing the destruction of myelin in the white matter of the brain and spinal cord, the myelin sheath of nerve trunks. Myelin acts as a sort of isolator, allowing the neuro-electrical impulses spread in certain directions. Its elimination leads to multiple "*short circuits*" in the process, which determines a particular clinical picture of the disease depends on the level of *"circuit"*.

Apheresis therapy, mainly plasmapheresis, removing from an organism such demyelinating agents, promotes if not recovery of the destroyed, then at least a slowing of the progression of these diseases, the stabilization of state [Keegan M. et al., 2002; Yücesan C. et al., 2007, 2008; Kaynar L. et al., 2008; Linker R.A., Gold R., 2008; Llufriu S. et al., 2009; Voinov V.A., 2010; McDaneld L.M. et al., 2010; Gwathmey K. et al.,

2011, 2012; Cortese I. et al., 2012; Heuchler M. et al., 2013; Rahmlow M.R., Kantarci O., 2013; Latov N., 2014; Ohkudo A. et al., 2014]. The plasma exchange with success is used and at emergence of the demylinating diseases at children [Kosiolek M. et al., 2013]. After plasmapheresis course (5-6 sessions up to 1,3-1,5 liters of plasma for each) there are signs of regression paralysis, impaired recovery of sensitivity, increase muscle strength. Repeated annual courses suspend the progression of the disease and improve quality of life for patients [Voinov V.A., 2010].

Let us examine some of these diseases in more detail.

Multiple sclerosis

MS - demyelinating disease of the central nervous system. It is an autoimmune inflammatory disease with diverse clinical manifestations, often leading to severe damage of motor activity, paralysis, vision loss, disorders of the pelvic organs. Although the etiology and pathogenesis are unknown, a number of features support the hypothesis about the role of as yet unidentified infectious agent that triggers an immune response against the distorted own nervous tissue, especially in genetically susceptible individuals. Although the antibody titers detected increase to various viruses (influenza, herpes simplex virus, Epstein-Barr virus, papilloma virus) in plasma and cerebrospinal fluid, but there is no clear guidance for the detection of RNA or viral antigens in the brain tissue itself. However, there are indications of the possible role of retroviruses in multiple sclerosis [Allain J.-P., 1998]. There is a chance of a process of molecular mimicry with the antigenic structure of individual proteins of viruses similar to the proteins of the brain tissue. In this case, a possible autoantigen is influenced by the excited viral antigens of T-lymphocytes, a myelin-oligodendrocyte-glycoprotein, breach of which may underlie the pathogenesis of multiple sclerosis [Bernard C.C.A. et al., 1997].

S. Sriram and collaborators (1997) mark as the main causes of multiple sclerosis T-lymphocytes, which penetrate into microglia and activate secretion and release of myelotoxic factors with direct damage to myelin in oligodendrocytes. Autoantibodies to MBP join in the processes of demyelination in the later stages of the development of multiple sclerosis [Vostrikova I.L. et al., 2006]. Activation of microglia cells also leads to the production of proinflammatory cytokines, chemokines, which in turn drives lymphocytes. In these processes there is also a release of "tumor necrosis factor", nitric oxide and free oxygen radicals, interleukins 1 and 12. Cytokines are detected and cerebro-spinal fluid. The content of IL12 can grow well in advance (4-6 weeks) to the exacerbation of the disease [van Boxel-Dezaire A.H.H. et al., 1999]. It is possible to believe that removal of such mediators of an inflammation by means of a plasma exchange promotes restoration of tolerance of immune cells to autoantibodies [Jamshidian A., Gharagozloo M., 2012]. It is possible to believe that removal of such mediators of an inflammation by means of a plasma exchange has to promote

restoration of tolerance of immune cells to autoantibodies [Jamshidian A., Gharagozloo M., 2012].

A number of patients with multiple sclerosis exhibit antinuclear autoantibodies characteristic of systemic lupus erythematosus which rather points to a systemic disease [Fukazawa T., 1997; Hashimoto H., 2010].

Demyelination process is not irreversible, as there is some "nerve growth factor" contributing to the restoration of myelin and nerve cell regeneration. However, the presence of autoantibodies against this factor in multiple sclerosis weakens the process, that is additional incentive for carrying out a plasma exchange.

Currently there are no known reliable methods of treatment that may inhibit the progression of the process. Based on the postulate of autoimmune nature of multiple sclerosis, we can use a lot of immunosuppressive and immunomodulatory agents - corticosteroids, azathioprine, and methotrexate, total irradiation of lymphocytes. There is known some effect of the oral administration of bovine myelin, resulting in reduction of autoreactive T-cells. Also used is intravenous administration of large doses of immunoglobulin. However, character of changes in the immunological multiple sclerosis status indicates immunodeficiency (decrease of T-lymphocytes and reduction ratio $CD4^+$ / $CD8^+$, decrease of IgM), glucocorticoids may therefore contribute further immunosuppression [Orlova Yu.Yu., 1999].

It is proved that injection of recombinant interferon β-1b promotes binding and neutralizing antibodies in some patients with multiple sclerosis [Ric G.P.A. et al., 1999; Plosker G.L., 2011]. However, anti-IFN-β molecules begin to form antibodies that reduce the efficiency of the drug [Majorga C. et al., 1999; Sorensen P.S., 2008; Applebee A., Panitch H., 2009; Zarkou S. et al., 2010]. In addition, there is a number of detected and serious side effects of such an interferon – the formation of subcutaneous abscesses at the injection site, liver problems, flu-like reaction, weakness, stomatitis, anorexia, decreased hemoglobin, neutrophils and platelets [Soria A. et al., 2007; Nakamura Y., et al., 2008; Okushin H. et al., 2010; Sanford M. et al., 2011; Mahe J. et al., 2013]. This often forces to interrupt this treatment [Clerio M. et al., 2008]. It should be taken into account relatively high cost of courses using interferon β-1b, reaching $400,000 [Bell C. et al., 2007].

Considered to be promising as well are selective inhibitors of adhesion molecules whose representative is a recombinant monoclonal antibody Natalizumab. Researchers revealed, however, a downside to this treatment – the development of progressive multifocal leukoencephalopathy [Clifford DB et al., 2010; Keene D.L. et al., 2012; Rudick R.A., 2011; Sørensen P.S. et al., 2012; Baldwin K.J., Hogg J.P., 2013; Boster A.L., et al., 2013; Eisele P. et al., 2014; Theódórsdóttir A. et al., 2014[. And, besides a natalizumab, leads treatment to such complication and other preparations on the basis of monoclonal antibodies – efalizumab, infliximab, adalimumab, etanercept, ibiritumomab tiuxetan, bevacizumab, alemtuzumab, cetuximab, brentuximab [Takao M.,

2013]. Also lethal outcomes of such complication after long reception of an efalizumab are described [Schwab N. et al., 2012]. At the same time, using plasmapheresis we had to remove the drug and to eliminate such complications thereby [Khatri B.O. et al., 2009; Schröder A. et al., 2010; Tan. I.L. et al., 2011; Takao M, 2013].

Along with this, the methods of therapeutic apheresis are used, plasmapheresis, in particular in combination with corticosteroids and cyclophosphamide [Khatri BO et al., 1991; Weinshenker BG, 2000; Ohji S., Nomura K., 2008; Schröder A. et al., 2009; Trebst C. et al., 2009; Hashimoto H., 2010; Magaña S.M. et al., 2011; Heuchler M. et al., 2013], and at the splenic perfusion (through a column with fragments of a spleen of a pig) promoting activation of T-lymphocytes at the expense of T-suppressors [Roth T.A., 1999], and cryo plasmosorption with processing in this way up to 2,5 volumes of the circulating plasma [Kreynes I.V., 1999]. However E.V.Nedashkovsky et al. (2003) note that use of a plasma exchange with extracorporeal modified autoplasma had no advantages before a usual not selective plasma exchange. Indications to a plasma exchange especially increase when pulse therapy by corticosteroids doesn't yield due result [Matsuo H., 2014]

V.I.Cherny et al. (2004) used the software plasmapheresis - 2 sessions per week, and then at 1, 3, 6 months, a year. Such tactics for 10 years, 7 patients allowed to achieve remission of multiple sclerosis. Carrying out such program plasma exchange was more effective than courses of a sporadic plasma exchange 1-2 times a year [Karpov M. I. etc., 2013]. We also prefer the tactics of the initial course of 4-5 sessions of plasmapheresis, followed by one session each month, which allows users to secure a positive result [Voinov V.A., 2014]. Success was achieved in the application of cascade plasmapheresis [Ramunni A. et al., 2008]. Positive results were achieved by selective Ig-apheresis with immunosorbents. I.M.Barbas and A.A.Skoromets (2003), the best results are achieved with courses of hemocarboperfusion.

Neuromyelitis optica

Neuromyelitis optica, or **Devic's disease** – inflammatory disease characterized by selective lesions of the optic nerve and spinal cord (extensive transverse myelitis with paraplegia). Previously it was considered as severe variant of multiple sclerosis. However NMO-IgG-antibodies, specific to this disease, a target for which is the aquaporin-4 (AQP4) which is in shoots of astrocytes or covering sites of the vessels which aren't covered with astrocytes legs, participating in formation of a blood-brain barrier are allocated. At its damage it doesn't cope with the function that promotes access and other immune components in CNS, in particular, of the leukocytes allocating toxic cytokines which complete death of oligodendrocytes and neurons [Argyriou A.A, et AL., 2008; Cree B., 2008; Marignier R. et al., 2010; Awad A., 2011]. Usually, primary, visual disturbances occur with subsequent addition of the symptoms of severe

transverse myelitis – a couple and tetrapareses, disorders of pelvic organs [Karim S., Majithia V., 2009]. Life expectancy thus usually doesn't exceed five years.

Used for the treatment are steroids, immunoglobulins and plasmapheresis to remove courses up to 2-3 liters of plasma per session [Greenberg B.M. et al., 2007;Watanabe S. et al., 2007; Bonnan M. et al., 2009, 2012; Magaña S.M. et al., 2009; Trebst C. et al., 2009; Caroll W.M., Fujiwara K., 2010; Ochi H., 2010; Wang K.C. et al., 2011; Devi B.V. et al., 2012; Khatri B.O. et al., 2012; Merle H. et al. 2012; Pula JH, MacDonald CJ, 2012; Sato D. et al., 2012; Morgan S.M., 2013, 2014; Cordoba J.P., 2014], followed by a periodically repeated sessions of plasmapheresis (program or intermittent plasmapheresis) [Miyamoto K., Kusunoki S., 2009]. S.H.Kim et al. (2013) note that after a plasma exchange course the level of antibodies to aquaporin-4 decreases to 15% of initial level, and the effect of treatment remains also in 6 months. This finds application and cascade plasmapheresis [Yoshida H. et al., 2010; Munemoto M. et al., 2011] and lymphocyte-apheresis [Nozaki I. et al., 2005]. Transversal myelitis can develop and against the system lupus erythematosis complicated by meningitis and the plasma exchange in that case also yielded positive result [Covach A.J., Rose W.N., 2014].

Guillain-Barré syndrome

This is an acute severe disease of the central nervous system, accompanied by progressive muscle weakness and paralysis, including respiratory muscles, which often requires prolonged mechanical ventilation. In such cases, when joining pneumonia, thrombocytopenia and bleeding, mortality can reach 12% [Netto AB et al., 2011]. At the heart of acute disseminated encephalomyelitis lie demyelinating processes. Its connection with chronic demyelinating diseases still debated, its pathogenesis is not clear, but the role of the immune system is undeniable.

Often, such a process is preceded by viral infections and vaccinations, sometimes an infection caused by Campylobacter jejuni [Straub J. et al., 1997; Hao Q. et al., 1999; Rogalewski A. et al., 2007]. At least 41% of patients identify this pathogen [Nachamkin I. et al., 1999]. Some connections are found for acute disseminated encephalomyelitis and previously suffered pneumonia caused by mycoplasma or bac. Legionella [Hagiwara H., et al., 2009; de Lau LM et al., 2010].

Detection of antibodies indicates a possible molecular mimicry between epitopes of the antigen of the infectious agent and the elements of the peripheral nerves, which determines the pathogenesis of this syndrome. Among the patients with this disease there is a large heterogeneity in the severity of neurological disorders of muscle weakness, the degree of sensory disorders, demyelination and axonal degeneration. Anti-GQ1b antibodies increases in severe ophthalmoplegia and Fisher syndrome, anti-GM1 antibodies are more concerned with purely motor variant of the disease, anti-GalNAcGD1a antibodies are detected more frequently in the gastro-intestinal infections

before clinical symptoms of Guillain-Barré syndrome with the development of distal paralysis [Hao Q. et al., 1999].

The widespread use of corticosteroids in the previous cases of treatment of Guillain-Barré syndrome has shown to be ineffective and was almost universally abandoned. In current methods of choice are plasmapheresis and intravenous immunoglobulin, and often a combination thereof. One group of researchers [Plasma Exchange / Sandoglobulin Gullain-Barré Syndrome Trial Group, 1997], considered it appropriate immediately after plasmapheresis treatment with IVIG at a dose of 0.4 g / kg, which should block the further development of antibodies. Total requires five sessions plasmapheresis with removal of 50 ml of plasma per kg of body weight. Although J. Tharakan et al. (1990) considered sufficient removal of plasma total of 10-15 ml / kg daily until a stable effect and regression of symptoms. Another group [The French Cooperative Group ..., 1997] prefers plasmapheresis. The same tactics are adopted and Quality Standards Subcommittee of the American Academy of Neurology [Hughes RA et al., 2003]. Japanese authors are of the opinion that plasmapheresis should be the method of choice in disseminated encephalomyelitis [Yuki N. et al., 1998; Shinozaki K. et al., 2008; Hagiwara H. et al., 2009].

Mild lesions (patients may walk more than 5 meters without assistance) is just two sessions of plasmapheresis, with moderate (the patient is unable to stand without support) and severe (need for mechanical ventilation) is required for 4 sessions of plasmapheresis [Kincaid J.C., 2002; Meena A.K. et al., 2011]. The same opinion was held by J.C. Raphael and collab. (1998), who believed that intravenous immunoglobulin for Guillain-Barré syndrome is ineffective. In such cases, there is preferred plasmapheresis [Buzzigoli SB et al., 2010; El-Bayoumi M.A. et al., 2011; Hughes R.A.C., 2011; Magaña S.M. et al. 2011].

It also describes and dramatic complication of this therapy for Guillain-Barré syndrome with intravenous immunoglobulin infusion at a dose of 0.4 g / kg of body weight – the development of acute severe allergic myocarditis with fatal outcome [Koehler PJ, Kondstaal J., 1996]. In the treatment of severe forms of this disease in children plasma exchange is more effective, but the technical difficulties of plasmapheresis in these patients forced to use medication immunoglobulins [Graf WD et al., 1994]. However, recent studies show a lower efficiency of immunoglobulin therapy compared to plasmapheresis [Dada MA, Kaplan AA, 2004; Lin CH et al., 2004]. In addition, the cost of five infusions of immunoglobulins is $ 10.329,85, while the cost of five sessions of plasmapheresis twice less - $ 4.638,16 [Winters JL et al., 2011]. All this forces to consider a plasma exchange as treatment of the first line [Kes P. et al., 2012].

It was possible to take the autoantibodies of IgG and IgM, passing the plasma received at a plasma exchange through columns with the covalent fixed tryptophan (immunosorption) [Haupt W.F., 2000].

Favorable results are received and when using equipment of a cascade plasma exchange [Valbonesi M. et al., 2001]. Nevertheless, in the analysis of results of use of courses of a plasma exchange (on 3 liters for a session) and a cascade plasma filtration, advantages of the last was revealed not [Lyi R. - K. et al., 2002].

It was possible to remove autoantibodies IgG, and IgM, obtained by passing through plasmapheresis plasma column with covalently fixed Tryptophan (immunosorption) [Haupt WF, 2000].

Favorable results were obtained using the technique of **cascade plasmapheresis** [Valbonesi M. et al., 2001]. However, when analyzing the results of the use of plasma exchange rates (at 3 liters per session), and the cascade plasma filtration, the advantages of the latter were not found [Lyi R.-K. et el., 2002].

In our practice even against a full tetraplegia, if we started carrying out a plasma exchange just at the first hours after developing of an illness, after the first session there are movements in extremities appeared, after the second or third – the patient can sit in a bed, after the fourth – to get on feet, after the fifth – can go. Thus, timely removal of antibodies allowed to restore a myelin but if treatment was late, on a place of a myelin usual connecting tissue which didn't possess the isolating properties any more was formed. And process passed into a chronic form [Voinov V.A., 2014].

Variants of Guillain-Barré are **Miller-Fisher syndrome** and **Bickerstaff brainsten encephalitis**. Sometimes they are combined under the name Fisher-Bickerstaff syndrome. The common feature is the appearance of IgG-antibodies to GQ1b with a picture of ataxia, areflexia and ophthalmoplegia [Hughes RA et al., 2007; Hussain A.M. et al, 2007; Lo YL, 2007; Yuki N., 2009; Meena AK et al., 2011]. In these cases the plasma exchange is effective also [Kuwubara S., 2014; Ejma M. et al., 2015].

Acute disseminated encephalomyelitis

It is a demyelinating disease with primary damage of white substance of a brain and spinal cord can develop in some days after a viral or bacterial infection or even vaccination [Garg R.K., 2002; Misra U.K., Kalita J., 2010]. There takes place an activation a myelin-reactive T-lymphocytes on the mechanism of a molecular mimicry. At MRT they find the centers of damage of white substance of the subcortical zones, the basal ganglions, a trunk, a cerebellum and a spinal cord. Most often children and young people suffer. Clinically there is a similarity to a debut of multiple sclerosis, however a further current more favorable after courses of high doses of corticosteroids with attraction and a plasma exchange also [Keegan M. et. al., 2002; Khurana D.S. et al., 2005; Llufriu S. et al., 2009; Alexander M., Mirthy J., 2011]. Acute demyelinnated encephalitis can be a consequence of antiviral vaccination (against diphtheria, tetanus, poliomyelitis, hepatitises A and B). Courses of a plasma exchange render favorable

effect, even in cases of their beginning in some weeks after emergence of the first symptoms [Rogalewski A. et al. 2007].

The **autoimmune autonomous gangliopaty** proceeds against orthostatic hypotension with the cognitive disorders which are also stopped by means of plasma exchange courses [Gibbins C.H. et al., 2012].

Acute encephalitis is also described caused by antibodies to called anti-N-methyl-D-aspartate receptor, at which developing convulsions, stupor, dysphagia and hypoventilation, until malignant catatonia. The use of high-dose prednisone does not give effect and signs of the disease have been cropped by a course of plasma exchange on the background of the rapid reduction of these autoantibodies [Schimmel M. et al., 2009; Chen B. et al., 2014; Mann A.P. et al., 2014; Morgan S.M. et al., 2014; Salvucci A. et al., 2014; Zhong J.M., 2014; Yongsiri S. et al., 2014].

Limbic encephalitis is a consequence of violations of carrying out electric impulses in synoptic potassium channels of the autoimmune nature. At the subacute beginning of a disease disorders of memory, a disorientation, hallucinations, the frustration of a dream which are giving in to plasma exchange courses against hormonal therapy are observed [Cunningham A.M. et al., 2014; Martin I.W. et al., 2014].

Acute polyneuropathy

To Guillain-Barré syndrome are close conditions of with the expressed muscular weakness which quite often develop at the patients with critical conditions (**ICU-acquired weakness**) demanding long artificial ventilation of lungs and complicating transfer of such patients to self-maintained breath. The electromyography shows thus an acute severe denervation and a neuromyopathy [Lipshutz A.K., Grooper M.A., 2013]. Biopsies of muscles and nerves indicate a serious neurogenic atrophy an axonal degeneration without inflammation signs. Such complications accompany patients with sepsis and multiple organ failure, after heart operations. Corticosteroids and neuromuscular blockers can be the provocative moments [Hund E.F et al., 1996; Dhand U.K., 2010].

In such cases the plasma exchange is also capable to stop such complications as the set of other toxic products collecting at patients in critical condition are at the same time brought out of an organism also [Algahtani H. et al., 2009]. It must be kept in mind that timely carrying out an extracorporeal detoxification can not allow developments of such complications. Probably that at such complications there comes the toxic demyelination. Thus, timely removal of antibodies allowed to restore a myelin but if treatment was late, on a place of a myelin usual connecting tissues which didn't possess the isolating properties any more was formed. And process passed into a chronic form [Voinov V.A., 2014].

Chronic inflammatory demyelinating polyneuropathy

It also develops as a result of auto-antibodies to gangliosides [Yuki N. et al., 1996]. The disease progresses for more than two months, and then weakness is retained, gradually accruing for months and years. Usually, this weakness is symmetrical, motor disturbances prevail over the disorders of sensitivity against areflexia [Lopate G. et al., 1997]. In some cases, developing so-called **POEMS**-syndrome characterized by **p**olyneuropathy, **o**rganomegaly, **e**ndocrinopathy, **M**-protein and **s**kin lesions.

In the treatment also preferred is plasmapheresis (2 sessions on the first three weeks and one session to the next three weeks). If necessary, repeat courses of plasmapheresis may be in the next 1 or 2 months, until the disappearance of the disease [Kincaid JC, 2002; Schröder A. et al., 2009; Yoon M.S., 2011; Gorson K.C., 2012; Latov N., 2014]. Also used is intravenous immunoglobulin (0.4 g / kg 1-3rd week and 0.2 g / kg in a 4-6-weeks). The effects of these methods are comparable. At 26% of patients there came full remission, with 61% - partial (could go) and only 13% remained incapable to go [Kuwabara S. et al., 2006]. Because immunoglobulin simpler and can be used at home, it is preferred as the initial treatment. In terms of value, they are also comparable. Steroids are available, but their long-term effects are more expensive [Dyck P.J. et al., 1994; Van der Meché F.G.A. et al., 1995]. Interferon β-1a use attempts didn't reveal its significant advantages [Hughes R.A. et al., 2010].

With the combination of polyneuropathy with **monoclonal gammapathy**, especially IgG and IgA type, an intensive course of plasma exchange resulted in a significant reduction in symptoms of muscle weakness, muscle buildup of potential patients become more mobile and return to them the ability to move independently [Dick PJ et al., 1991; Brannagan T.H., 2009]. Plasmapheresis in this pathology has been successfully used in pediatric practice [Rabie M., Nevo Y., 2009]. A good result was achieved after a **cascade plasmapheresis** [Chiu HC et al., 1997; Hanafusa N. et al., 2007].

Paraproteinemic demyelinated polyneuropathy

It develops in the presence of the monoclonal hyperproteinemia accompanying amyloidosis, POEMS syndrome, a cryoglobulinemia, a multiple myeloma, the B-cellular lymphoma and Waldenström's macroglobulinemia. Thus appear an autoantibodies against the myelin-connected glycoproteins of peripheral nerves [Rajabally U.A., 2011; Lunn M.P., Nobile-Orazio E., 2012; Ramchandren S., Lewis R.A., 2012].

At a polyneuropathy combination to a **monoclonal gammapatia**, especially IgG and IgA of types, carrying out an intensive course of plasma exchange led to considerable reduction of manifestations of muscular weakness, increase of muscular potentials, patients became more mobile and to them ability independently to move came back [Brannagan T.H., 2009]. The plasma exchange at this pathology with success was used

and in pediatric practice [Rabie M., Nevo Y., 2009]. And, efficiency of a plasma exchange was higher, than steroid therapy [Kimura A. et al., 2010]. The good result was reached and after a cascade plasma exchange [Chiu H.C. et al., 1997; Hanafusa N. et al., 2007].

Chronic motor neuropathy

It is - a slowly progressive disorder of the peripheral nerves, which leads to an asymmetrical weakness of the distal upper extremity. Electromyographic patterns shows focal blockade of transmission of impulses along the motor axons. In contrast of amyotrophic lateral sclerosis, this immunodependant disease proceeds with demyelination, and treatable by plasmapheresis together with cyclophosphamide [Kornberg A.J., Pestronk A., 1995; Claus D. et al., 2000; Park Y.E. et al., 2010].

The content of IgM-antibodies to GM1-ganglioside is found in 85% of patients [Pestronk A., Choksi R., 1997]. The pathogenesis of neuropathies can participate IgM M-protein, often having autoantibodies activity. IgM M binds myelin-associated glycoprotein, which leads to demyelination of peripheral nerves. Plasma exchange is also considered one of the methods of elimination of IgM M [Latov N., 1995; Park Y.E. et al., 2010].

Lewis-Sumner's syndrome which is characterized by sensory-motor deficiency of the top extremities because of a demyelination is close to the previous pathology. The plasma exchange is also effective in its treatment [Park Y.E. et al., 2010].

Myasthenia gravis

In this cases of IgG antibodies appear to nicotine acetylcholine receptors postsynaptic membrane, which leads to increasing muscle weakness [Lindstrom JM et al. 1998].]. In some cases perhaps the antibodies emergence also to a muscle specific kinase [Yamada C. et al., 2014]. In this case, the direct removal of antibodies by plasmapheresis is very effective [Lehmann H.C. et al., 2006; Zagar M. et al., 2009; Ganeev T.S. et al., 2013; Dasararaju R. et al., 2014; Yamada C. et al., 2014]. It is made to promote the normalization of immunoglobulin levels and reduction of the circulating immune complexes (CIC) of 1.7 - 2 times. In severe cases, patients can be quickly disconnected from the ventilator, but it is a relatively short-term effect and requires fixing repeated sessions [Levis R.A. et al., 1995; Kosachev V.D. et al., 2006].

However, along with plasmapheresis, the same results are reached via intensive intravenous immunoglobulin therapy at a dose of 0.4 g / kg daily for three or five days [Gaidos P. et al., 1997; Barth D. et al., 2011]. Nevertheless, with intensive plasmapheresis we can achieve better results in the treatment of myasthenic crises, rather than intravenous administration of immunoglobulins, which cost of a course makes $78.814 [Myasthenia Gravis Clinical Study Group ..., 1997; Fleury MC, Tranchant C., 2008; Gold R., Schneider-Gold C., 2008; Tranchant C., 2009; Heatwole

C. et al., 2011; Hellman M.A. et al., 2014; Liew W.K. et al., 2014; Morgan S.M. et al., 2014].

It is advisable to carry out 3-5 sessions of plasmapheresis with removal of plasma up to 2.0-2.5 ml / kg body weight [Köhler W. et al., 2011]. Carrying out and daily sessions of a plasma exchange with removal of smaller volumes of plasma, than such plasma exchange, carried out every other day is possible [Trikha I. et al., 2007]. Similarly, the use of plasma exchange provide faster positive effect (after the first session already) in patients refractory to rituximab [Nowak RJ, 2011]. Plasmapheresis before surgery thymectomy greatly facilitates the postoperative period [Nagayasu T. et al., 2005; Yeh JH et al., 2005; Gold R. et al., 2008; Konishi T., 2008; El-Bawab H. et al., 2009].

With juvenile forms of myasthenia gravis is also successfully used plasmapheresis with immunoglobulins [Anlar B. et al., 2009; Chiang L.M. et al., 2009; Papazian O., Alfonso I., 2009], and W.K.Liew et al. (2014) noted that the plasma exchange yields stabler results, than IVIG therapy.

Prospects are seen in the use of specific IgG-immunoadsorption to remove antibodies to acetylcholine receptors [Zisimopoulou P. et al., 2008] as well as new systems for the cascade plasmapheresis [Chuang YC et al., 2000; Batocchi A.P. et al., 2000; Yeh J.H. et al., 2001, 2003, 2005; Konishi T., 2008]. At a cascade plasma exchange the level of soluble molecules of intercellular adhesion decreases more effectively and the quantity of the T-regulating cells increases [Zhang L. et al., 2014]. After a cascade plasma exchange the increase in the $SatO_2$ levels with decrease in pCO_2 is observed [Yeh J.H. et al., 2013].

Nevertheless, J.H. Yeh H.C.Chiu (2000), and later by R. Pittayanon et al. (2009) compared the comparable groups of patients with myasthenia noted no significant differences in the effectiveness of immunoadsorption or cascade plasmapheresis. On the other hand J.F.Liu et al. (2010) observed no benefits immunoglobulin transfusions before cascade plasmapheresis or immunoadsorption. After a cascade plasma exchange also decrease in cytotoxic activity of the natural killer cells is noted that even more strengthens effect of such treatment [Chien P.J. et al., 2011].

Myasthenic Lambert-Eaton syndrome

It is a rare disease that occurs as a result of the blockade of the presynaptic release of acetylcholine in the nerve ending (at the neuromuscular synapse). Interestingly, half of patients was with lung cancer. Diagnosis is based on electromyography. Recent evidence suggests an autoimmune impact directly against the momentum of the electrical installation in the calcium channels at the presynaptic motor nerve terminal [Leys K. et al., 1991]. Used in the treatment of immune suppression are improving agents conducting electrical discharge in the nerve terminal. Plasmapheresis leads to improvements in the majority of patients, but requires repeated sessions on

immunosuppressive therapy [Dau PC, Denys EH, 1982; Sanders DB, 1995; Ueda T. et al., 2009; Titulaer M.J. et al., 2011; Gwathmey K et al., 2012]

"Paraneoplastic" autoimmune diseases of the central nervous system.

The term "paraneoplastic" refers to the processes that accompany certain types of tumors, especially ovarian and breast cancer. The presence of specific anti neural antibodies in these patients supports the theory autoimmune origin of these disorders. There are refered to antibody staining of Purkinje cells cytoplasm. On the other hand, the detection of such antibodies in patients with neurological symptoms of cerebellar degeneration was a highly specific marker for the presence in them of not yet diagnosed tumors.

J.W.B. Moll and collab. (1996) studied presence of antibodies, both anti neural and "systems" (vs. DNA mitochondria thyroid antigens, rheumatoid factors), in patients with paraneoplastic syndrome, and in patients with small cell lung cancer, ovarian cancer and breast cancer, but no evidence of this syndrome, and a control group of healthy individuals. It was found that the "systems" autoantibodies were found in 52% of patients with paraneoplastic syndrome compared with 16% in the isolated tumors and 15% in the control group. Thus, the relatively high frequency of systems autoantibodies in patients with paraneoplastic syndrome indicates some genetic predisposition to autoimmune phenomenon. This explains the rare incidence of this syndrome in cancer patients (i.e., the syndrome is implemented in cancer patients with a predisposition to systemic autoimmune diseases).

The manifestations of this syndrome can be smoothed both after removal of the tumor and in immunosuppressive therapy, including plasmapheresis [Dropcho E.J., 1995; Armstrong M.B. et al., 2005; Schröder A. et al., 2009; Agrawal S. et al., 2010; Mirza M.K. et al., 2011; Pham H.P. et al., 2011; Chen B. et al., 2014]. Thus, Y. Ben David et al. (1996) observed a significant improvement in neurological manifestations in patients with ovarian cancer and cerebellar degeneration after a course of plasmapheresis, although F. Graus et al. (1992), this result is not obtained. A.M. Landtblom et al. (2008), conducting courses in 3 sessions (a total of 22 per year), was also prepared with only a temporary effect.

Could develop such a rare variety of paraneoplastic syndrome may develop as melanocytic proliferation of choroid, also treated with plasmapheresis [Jaben EA et al., 2011].

Amyotrophic lateral sclerosis

It is a relentlessly progressive neurological syndrome in which there is destruction of motor neurons, leading to increasing weakness of the facial muscles and limbs, atrophy with spastic symptoms, hyperactivity reflexes, respiratory failure and imminent death within three years. The detection rate – 1-3 per 100 000 population. Some patients have

antibodies influencing the conduction of impulses through the calcium channels of neuromuscular synapses, which leads to motor neuron disorders and swelling of the fragmentation of the Golgi apparatus [Offen D. et al., 1998].

In addition, the detected small infiltrates of T-cells in the brain and spinal cord to the possible spread of their influence on neighboring motor neurons, as well as complement keeping immune complexes in the neuromuscular synapses. The autoimmune nature of the disease is often reinforced by the concomitant autoimmune disease of the thyroid gland and paraproteinemia. Unsuccessful attempts to use immunosuppressive therapy does not rule out the genesis of autoimmune disease [Smith RG et al., 1996].

According to some reports in the genesis of the disease may play a role and exogenous factors. For example, one of the spread of disease endemic areas in Guam (New Guinea) patients showed high concentrations of aluminum and manganese, with reduced calcium. In motor neurons it was detected accumulation of hydroxyapatite aluminum. Due to lysis of infected cells there can be a formation of antibodies to the nerve fibers. Metal complexes in neurons may be found for many years, and then for unknown reasons signs develop of amyotrophic lateral sclerosis or Parkinson's disease with dementia syndrome. In the cerebrospinal fluid also showed increase of glutamate and aspartate, which may damage the motor neurons [Popova L.M., 1998].

Given the widespread use of aluminum-containing tap water purification reagents, such a possibility is not excluded in our cities, which underlines the need for the use of a variety of household water filters and therapeutic apheresis, able to promptly withdraw excessive amounts of aluminum and other potentially harmful metals to prevent such disorders. And reports appeared on the successful use of plasmapheresis treatments at intervals of 1-2 months for 12 years, which provided a stable condition of the patient [Gorshkova N.N., Volkova V.N., 2003]. Success of use of a plasma exchange was achieved also by P. Kenarov et al. (2014). The patient who couldn't pass also meter without support, began to pass freely to hundred meters and to drive the car.

Charcot-Marie-Tooth disease

It is the most widespread hereditary and degenerate disease of peripheral nervous system. Its symptoms usually start being shown in the late childhood or early youthful age. Some patients have no symptoms until they reached age thirty or forty years. Usually main symptoms connected with difficulties of dorsal bending of foot and a shin. It can also cause deformation of feet and a shin with fingers with an unusual helicoid form. Muscles are atrophied in the lower part of a foot. In process of progressing of an illness, many patients appear also weakness in hands and forearms. Symptoms and the course of a disease can be various. In certain cases there can be a breath violation, a hearing disorder, sight, weakness in a neck and humeral muscles. Scoliosis is the widespread phenomenon. Emergence of gastrointestinal disorders, difficulties is possible during the chewing, a swallowing and the speech. The atrophy of muscles can

lead to a tremor [Dyck P.J. et al., 2005; Rossor A.M. et al., 2013; Saporta M.A., 2014]. Still enough effective methods of treatment of this disease aren't found [Baets J. et al., 2014].

Nevertheless, P. Kenarov et al. (2014), having applied regular courses of a plasma exchange, reached very notable results. After six courses of a plasma exchange made with intervals three and six months for the last three years it is registered: restoration of sight with 6 to 2 dioptries; continuation of restoration of a voice and absence of fatigue at speech loading (the patient – the teacher); restoration of sensitivity in extremities – the patient feels a touch, heat, cold and pain; restoration of motor functions in hands and feet – independently walk alone, without restriction; also signs of an autoimmune thyroiditis was disappeared.

Children's autoimmune neuropsychiatric disorders

They caused by a streptococcal infection and a **Sydenham's chorea** or small chorea (in the past "**Saint Vitus Dance")** are shown by fast in-coordinate twitchings of face muscles, hands and feet, up to a catatonia. Arises more often at children against a streptococcal infection at 20-30% of patients with acute rheumatic fever. Thus, antibodies, against a streptococcal M-protein cross react with anti-genes of neurons of a basal membrane (effect of "a molecular mimicria"). Illness symptoms quite often appear in 4-8 weeks after streptococcal pharyngitis [Heubi C., Shott S.R., 2003; Gabbay V. et al., 2008]. As well as at other rheumatic diseases, this disease of also autoimmune nature and a plasma exchange renders medical effect [Garvey M.A. et al., 2005; Lopez Y. et al., 2007; Cortese I. et al., 2011; Schwartz J. et al. 2013].

Morvan fibrillary chorea

It is characterized by generalized myokymia (pseudo fasciculations), pain, hyperhidrosis, weight loss, insomnia, and hallucinations. The disease develops as idiopathic and due to mercury intoxication, chrysotherapy (treatment with salts of gold) and thymoma. The pathogenesis of the primary forms of the disease remains unclear, although by analogy with similar diseases that are accompanied by increased muscle activity not to be excluded is autoimmune nature of the disease. An indirect confirmation of this view is the highest reported case of repeated sessions of plasmapheresis that stops the main manifestations of the disease [Madrid A. et al., 1996].

Stiff-man syndrome

This is progressive encephalomyelitis with muscular rigidity – a rare but serious autoimmune disease, with increasing bulbar hyper contracture, diplopia, dysphagia, pain in areas of the spastic muscle contractions. For these patients typical thing is hyperlordosis. Diazepam is used in the treatment, significantly reducing motor activity, as well as baclofen and hlonazepam.

It is hypothesized that this syndrome is the result of an imbalance between inhibitors of γ-aminebutyl acid α-motor neurons. There are signs that the autoantibodies of patients Stiff-man syndrome, cerebellar ataxia and diabetes mellitus type 1 react with glutamic acid decarboxylase, the synthesizing enzyme, which is localized in the corresponding neurons [Saiz A. et al., 1997; Abele M. et al., 1999; Tuomi T. et al., 1999; Rakocevic G., 2012; Farooqi M.S. et al., 2015].

Plasmapheresis, reducing the titer of antibodies, reduces extraceptive reflexes, decrease in muscle motor activity and provides significant clinical improvement [Brashear HR, Phillips LH, 1991; Shariatmadar S., Noto TA, 2001; Schröder A. et al., 2009; Farooqi M.S. et al., 2015]. L. Fogan (1994) also noted that the use of plasmapheresis with subsequent courses of corticosteroid therapy resulted in a significant improvement and long-term remission. ASFA also allows application of a plasma exchange at this pathology [Schwartz J. et al., 2013].

Acquired neuromyotoniya

As the previous pathology, it is a rare disease of unknown etiology in which hyperexcitability of peripheral motor nerves leads to involuntary muscle twitching, painful spasms and weakness. Given the possible mechanism of autoimmune disease, S. Sinha et al. (1991) after 7 years of ineffective drug therapy, using plasmapheresis, which each time resulted in the almost complete disappearance of the symptoms for 2-3 weeks with a very pronounced decline recorded electromyographic neuro myotonic disorders. Over the next few weeks, the symptoms slowly returned.

Rasmussen's encephalitis

It is a rare syndrome of progressive unilateral brain disfunction with limited seizures. Usually occurs in childhood (6-8 years old), with a gradual progression, resulting in hemiparesis and dementia. Revealed are signs of inflammation with perivascular accumulations of lymphocytes. The autoimmune nature is proved by detection of autoantibodies. In some cases, improvement was reached with the use of corticosteroids and immunoglobulins. However, resulting in a significant improvement was a course of plasmapheresis (5-6 sessions of up to 1 circulating plasma volume each). In this case, convulsions stopped, there was improvement in speech and motor activity [Andrews PI et al., 1996].

Autoimmune autonomic gangliopathy

It accompanied by a lesion of both the nerve fibers and ganglion. As of intravenous immunoglobulin therapy and plasma exchange offer improvement of the clinical picture of lesions [Iodice V. et al., 2009].

Fatal familial insomnia

It is a rare but severe genetically determined disorder characterized by a significant shortening of sleep time and is accompanied by increasing weakness, impaired autonomic functions, ataxia, dysarthria, hallucinations, delirium and myoclonus. Starting at the age of 25-60 years, continues from 7 to 33 months, with the imminent deaths [Gambetti P., Parch P., 1999].

This disease is a kind of **"prion" diseases”**. Prions are proteins that are normally soluble in detergents, have the form of α-helix and are protease-destroyed. Pathological β-isoforms have a flattened shape, insoluble and resistant to proteases. With their accumulation there is possible development of such pathological insomnia. Thus there is a loss of neurons in the thalamus astroglial proliferation, olivas and the cerebellar cortex [Mastriani JA et al., 1999].

The prion etiology is characteristic and for **Creutzfeldt-Jacob's disease** with spongious encephalitis and quickly progressing dementia. Thus increase of the maintenance of various cytokines and oxidants aggravating damage of a brain comes to light [Burwinkel M. et al., 2004; Geschwind M.D. et al., 2008; Riemer C. et al., 2009]. To treatment such diseases don't move, however, as well as at others "accumulation diseases", therapeutic apheresis can be rather effective.

Parkinson's disease

It is a progressive neurodegenerative disorder primarily with motor dysfunctions. Aetiopathogenesis of it is not entirely clear, though there is evidence of the presence of autoimmune disorders. Revealed are elevated levels of cytokines and complement in the cerebrospinal fluid increases against T-cell autoantibodies (anti-alpha-synuclein and anti-GM1-ganglioside) and vasoactive peptides in peripheral blood [Staines DR, 2007; Monahan AJ, 2008; Benkler M et al., 2009]. This points to the possibility of using plasmapheresis in the treatment of this disease [Leopold NA et al., 1999; Staines D.R. et al., 2008]. S.G.Morozov et al. (1997) successfully perform courses of plasmapheresis in 29 patients with severe manifestations of Parkinson's disease with a decrease in the index of neuro defeciency from 28 to 8 units of Webster scale and levels of autoantibodies.

Chronic fatigue syndrome

It can be found in 267 persons per 100 000 of population. It is accompanied by progressive weakness and physical exhaustion, reduced endurance, neurological complications and immune dysfunctions [Staines D.R., 2006]. So far there is no clear or clinical or ethio- or pathogenetic mechanisms. Some manifestations of this syndrome suggest an autoimmune mechanism of its development. 52% of patients showed responses to nuclear antigens. Autoantibodies were of IgG-isotype. There are cases of abnormalities and dysfunction of T-lymphocytes. The presence of the circulate immune complexes and antinuclear antibodies was detected in over 30% of patients. It is

possible that immune disorders occur in response to certain chronic infection [Fernandéz A.A. et al., 2009]. There are founded also a high level of pro-inflammatory cytokines [Lorusso L. et al., 2009]. All of this points to the possibility of plasmapheresis for treatment of this disease Voinov V.A., 2010].

Toxic polyneuropathy

They develop as a result of a number of the acute and chronic intoxications accompanying diphtheria, intensive chemotherapy of tumors (cysplatin, vincristine, paclitaxel, oxaliplatin and bortezomib), alcoholism, a consequence of pesticides, industrial and food toxicants [Misra U.K., Kalita J., 2009; Boyette-DavisJ.A. et al., 2015]. In such cases the plasma exchange also renders a positive effect.

Alzheimer's disease

It is a common disease of the elderly, affecting up to 29 million people in the world [Davis RM et al., 1999]. It is characterized by extracellular deposits in the brain aggregates 39-43 amino acid peptide called β-amyloid and increasing loss of neurons with 75-kD neurotrophic receptors. It was found that β-amyloid binds these receptors, which leads to inevitable loss of these neurons [Yaar M. et al., 1997]. There comes a gradual degradation of the individual, amnesia, impaired motor coordination, and paralysis. Disorders of consciousness in Alzheimer's disease can be detected in 1% of people younger than 65 years, but they amount to 50% for the 85 years of life [Mecocci P. et al., 1998].

It is believed that a significant role is played in the pathogenesis of progressive mental disorders by mutational immunopathological mechanisms of degradation specific protein structures - "presenilin-1" with a high accumulation of amyloid substance β-polymerized and *tau* protein extracellularly as well as in the frontal lobes intraneuronal with neuro-changes in their fibrillar structure [Beyreuther K., Masters CL, 1997; Gómez-Isla T. et al. 1997; Levey A.I. et al., 1997]. When this occurs immunoprecipitation β-amyloid specific endoplasmic reticulum associated protein that promotes damage of cell membranes and the stimulation of active oxygen radicals, resulting in the death of these cells [Yan SD et al., 1997]. In addition, β-amyloid and special senile plaques deposited in the cerebral vessels. In this case, partially penetrate the senile plaques in the vascular wall, and β-amyloid cylindrically surrounds the vessel, narrowing the lumen [Uchihara T. et al., 1997]. In Alzheimer's disease patients exhibit elevated levels of apolipoprotein E, which indicates the proximity of such a pathology with "vascular dementia» [Marin DB et al., 1988]. There is a large role of activation of the complement proteins produced by cells of the microglia, astrocytes and pyramidal neurons [Terai K. et al., 1997]. Perlecan enhances this process - a specific heparan sulfate proteoglycan that accumulates in the β-amyloid fibrils [Castillo G. et al., 1997]. The structure of amyloid deposits include not only amyloid β, but other so-called amyloid-associated proteins composed of

complement regulatory factors and proteolytic enzymes, apolipoprotein E and other components [Aizawa Y. et al., 1997].

The predecessor of β-amyloid (β-APP) is a multifunctional protein that is widely represented in the nervous system. This precrusor (β-APP) is transported along the axons and accumulates in presynaptic terminals and "points of growth". β-amyloid, is released enzymatic from β-APP, has a tendency to form fibrils, damaging neurons and increases their vulnerability. This mechanism involves the generation of oxygen radicals and damage to membrane transport systems [Mattson MP, 1997].

There are signs of permeability of blood-brain barrier facilitating penetration as amyloid proteins in brain tissue, and the reverse transition of neurospecific protein into the systemic circulation, where they fall into the "field of vision" of the immune system and stimulate the formation of autoantibodies to affect not only against these proteins but similar protein structures of the central nervous system.

Among pathogenetic factors of Alzheimer we detected the role of oxidative stress and the accumulation of free radical molecules, affecting not only the structure of the brain, but also the peripheral cells, including lymphocytes [Mecocci P. et al., 1998]. At the same time, use of antioxidants doesn't influence the maintenance of an amyloid and tau-protein [Galasko D.R. et al., 2012]. Attempts of use of statin also didn't lead to improvement of cognitive functions and didn't prevent progressing of an illness [Feldman H.H. et al., 2010; Sano M. et al., 2011].

Causes and treatment of this serious disease of the brain are unknown, but the above facts indicate that the autoimmune nature of the disease of "accumulation" and unequivocally put a question on the possibility of using methods of apheresis therapy, at least to slow the progression of this severe illness with a bleak prognosis and in recent years some have described the successful experience of plasma exchange with replacement of removed plasma with albumin [Boada M. et al., 2009; Boada-Rovira M., 2010; Roca I., Cuberas-Borros G., 2010]. This is based on the fact that 90% of the circulating beta amyloid associated with albumin and after plasmapheresis the donor albumin mobilizes of brain amyloid, thereby contributing to the improvement of cognitive functions in these patients [Anaya F., 2010].

Possible is the development of **autoimmune dementia**, where hormone therapy, including plasmapheresis, has a positive effect [Flanagan EP et al., 2010].

Ischemic attacks and ischemic strokes in many cases are the consequences not only of atherosclerosis, but also **antiphospholipid syndrome** [Greenberg SM, Hyman BT, 1997]. Probability of the latter increases with the occurrence of a disease at a young age that redefines treatment policy conventional in such cases, increasing the anticoagulant therapy with attracting and apheresist methods. Amount of anticardiolipin antibodies increases with age from 60 to 70 years, as well as in patients with diabetes and hypertension, which does not exclude the influence of the mechanisms of

autoimmune disorders of cerebral circulation [Tanne D. et al., 1999]. Furthermore, after acute cerebral stroke period there are detected autoantibodies to myelin basic protein [Evdokimov A.V., Gerasimova M.M., 2006]. There is information of occurrence of vascular lesions of the brain on the type of vasculitis on the basis of the appearance of autoantibodies to myeloperoxidase, which are markers of vasculitis. Marked increase in 2-3 times the level of antiphospholipid autoantibodies in patients with vertebral-basilar circulatory insufficiency, especially with its prolonged duration [Fomina L.A., Gerasimova M.M., 2006].

All of this allows us to consider plasmapheresis very promising for vascular diseases of the central nervous system and its wide application is a matter of the near future. Indeed, even a course of plasmapheresis in the acute phase of ischemic stroke on the basis of the antiphospholipid syndrome enables quick regression of speech and of brain disorders [Elchaninov A.P. et al., 2003]. Y. Hasegawa et al. (2003) using cascade plasmapheresis for 5-7 days after a stroke on the basis of the middle cerebral artery occlusion achieved reduction in plasma viscosity and a significant increase in cerebral blood flow from 36.4 to 40.7 ml/100g/min on the affected side with the rapid regression of hemiplegia almost immediately after the procedure. Plasma exchange was effective for acute stroke on the basis of thrombotic thrombocytopenic purpura [Sevy A. et al., 2011].

We cannot exclude any autoimmune or metabolic disorders in the genesis of **diencephalic syndrome** and some other kinds of **neurotic disorders** - or neuro vascular dystonia, and neurological disorders can carry not a primary but secondary. This could be seen in detectable shifts of hormonal and neuro-mediator regulation.

Migraine

There is also quite a severe, though not fatal, disease which is not amenable to conventional therapeutic effects, followed by an abrupt onset of severe headache with nausea and vomiting. Pathological processes of this disease may be similar in nature to atopic allergy, especially since it such as paroxysmal local Quincke's angioedema. When migraines are also likely to arise is a crisis violation of local vascular permeability with edema of the relevant department of the brain, the more that headache often also has a local character (for example - the left parietal region). Biologically active substances cause histamine release and proteolytic enzymes that convert inactive kininogens in plasma kinins and other active substances that may cause pain.

It is possible to find in such patients also anti-phospholipid antibodies (anticardiolipin antibodies and lupus anticoagulant), especially in cases of the accompanying passing neurologic disorders at migraine with aura [Tietjen G.E. et al., 1998]. Obesity and diabetes from the metabolic disorders can be another possible reason [Bhoi S.K. et al., 2012]. These reasons also do indicated apheresis therapy. So, A. K. Marchuk and N. M. Bulanova (2001) report that after a plasma exchange it was succeeded to stop a

migraine attack with normalization of aggregation activity of platelets and increase of level of a cortisol.

Such patients can help detect antiphospholipid antibodies (anticardiolipin antibodies and lupus anticoagulant), especially in cases of transient neurological disorders associated with migraine with aura [Tietjen GE et al., 1998]. These packages also make the indications for apheresis therapy. So, A.K.Marchuk and N.M.Bulanova (1999) reported that after plasmapheresis could stop an attack of migraine with normalization of platelet aggregation and increased levels of cortisol.

Refsum's disease

It is the result of accumulation of phytin acid and is characterized by loss of sense of smell, hearing, retinitis pigmentosa with loss of vision (night blindness), ichthyosis, ataxia and symptoms of chronic polyneuropathy. In the future, what can join is heart failure on the basis of cardiomyopathy. In the treatment, in addition to a diet that excludes the reception of phytin acid, in severe cases of increasing weakness and arrhythmias is used and plasmapheresis also [Wanders RJA et al., 2010; Perera N.J. et al., 2011].

Tick-borne encephalitis (TBE)

Severe consequences are suffered from **Ixodes ricinus ticks**. It is the most important viral tick-borne disease in Europe and can cause severe disease in humans and might be more widespread than the distribution of reported human cases suggests [Paulsen K.M. et al., 2015]. The majority of cases remain undiagnosed, also because of the lack of diagnostic serology, as there is no routine screening for TBE in non-endemic regions [Haditsch M[1], Kunze U., 2015]. With ticks bite of Ixodes ricinus Borrelia burgdirferi spirochetes are transferred. There is developed leptomeningitis, vasculitis and focal inflammations in the central nervous system, the necrotizing focal myelitis in cervical spinal cord, radiculitis, neuritis and a demyelination in the spinal roots [Ramesh G. et al., 2015]. Borreliya induce secretion of interleukins (IL-4, IL-10, IL-12, IL-1β, IL-6, IL-8, TNF-α, IFN-γ), macrophages inflammatory protein of MIP-1α and MIP-1β, and chemokine eotaxin, possessing toxic properties [Widne M. et al., 2002, 2004; Sjöwall J. et al., 2005; Nordberg M. et al., 2011; Konkovo A.B., Ratnikov L.I., 2012]. At borreliosis the maintenance of IFN-γ, promoting lysis and elimination of Borrelia burgdorferi accrues, but it is the reason and tissue damages [Ekerfelt C. et al., 2003].

Already in the acute stage of the disease develop severe brain damage with symptoms and multiple organ disorders – a toxic cardiomyopathy, and hepato-renal failure, which in turn is reflected in the activity of the central nervous system, up to a lethal outcome [Misić-Majerus L et al., 2005]. In later period of an illness there are damages of joints (Lime arthritis) [Yin Z. et al., 1997] and chronic atrophic acrodermatitis [Blaise S. et al., 2014]. So there is a chain reaction in the process of developing the disease. This in itself calls for measures to detoxify.

On the other hand, as a result of destruction of neurons and other structures of the nervous system under the influence of viruses translocation happens of autoantigens previously hidden from the immune system that causes the formation of autoantibodies and immune complexes. In the transition to the chronic form of the disease entering these autoantibodies and immune complexes in the brain is supported by degenerative processes which started there [Shapoval A.N., 1980]. There is an additional indication for program plasmapheresis at such consequences of ixodes encephalitis.

To summarize the description of nervous diseases, it is necessary to emphasize that virtually all of the above components of the pathogenesis of autoimmune diseases are in some degree confirmed by the results of numerous studies, which means that the plasmapheresis should take their proper place in the complex therapy. Presented are specific examples of the successful use of plasmapheresis with one hand and certain risks and side effects of alternative therapies. In conclusion, we present results of a multicenter analysis of long-term experience with the use of plasmapheresis in nervous diseases, presented by the American Academy of Neurology [Assessment of plasmapheresis, 1996].

Indications for plasmapheresis, established by the American Academy of Neurology

Disease	Settings
Guillain-Barré syndrome, severe form	Defined
Chronic inflammatory demyelinating polyneuropathy	Defined
Polyneuropathy with monoclonal gammapathy the possible role played by:	
IgG/IgA	Defined
IgM	In study
Myasthenia gravis: in preparation for operations or stroke	Defined
Myasthenic syndrome of Lambert-Eaton	Use possible
Acquired neuromyotoniya	In study
Stiff-man syndrome	In study
Cryoglobulinemic polyneuropathy	In study
CNS damage during lupus	In study
Acute disseminated encephalomyelitis	In study
Multiple sclerosis	Use possible

In addition, in this analysis presented is data on value of plasmapheresis - from $1,000 to $2,000 per treatment, and the rate of five such sessions can cost $5,000-10,000. But, on the other hand, a course of intravenous immunoglobulin-therapy also costs about $10,000.

These positions have not changed significantly later [Cortese I. et al., 2011].

Sources

Abele M., Weller M., Mescheriakov S. et al. Cerebellar ataxia with glutamic acid decarboxylase autoantibodies // Neurology. – 1999. – Vol. 52, № 4. – P. 857-859.

Algahtani H., Moulin D.E., Bolton C.F., Abulaban A.A. Guillain-Barre syndrome following cardiac surgery. Difficult diagnosis in the intensive care unit // Neurosciences (Riyadh). – 2009. – Vol. 14, № 4. – P. 374-378.

Allain J.-P. Emerging viruses in blood transfusion // Vox Sang. - 1998. - Vol. 74, Suppl. 2. - P. 125-129.

Andrews P.I., Dicter M.A., Bercovic S.F. et al. Plasmapheresis in Rasmussen's encephalitis // Neurology. – 1995. – Vol. 46, № 1. - P. 242-246.

Anlar B., Yimaz V., Saruhan-Direskeneli G. Long remission in muscle-specific kinase antibody-positive juvenile myasthenia // Pediatr. Neurol. – 2009. – Vol. 40, № 6. – P. 455-456.*Applebee A., Panitch H.* Early stege and ling term treatment of multiple sclerosis with interferon-β // Biologics. – 2009. – № 3. – P. 257-271.

Assessment of plasmapheresis. Report of the therapeutics and technology assessment subcommittee of the AMERICAN Academy of neurology // Neurology. – 1996. – Vol. 47, № 3. – P. 840-843.

Batocchi A.P., Evoli A., Di Schino C., Tonali P. Therapeutic apheresis in myasthenia gravis // Ther. Apher. – 2000. – Vol. 4, № 4. – P. 275-279.

Bell C., Graham J., Earnshaw S. et al. Cost-effectiveness of four immunomodulatory therapies for relapsing-remitting multiple sclerosis: a Markov model based on long-term clinical data // J. Manag. Care Pharm. – 2007. – Vol. 13, № 3. – P. 245-261.

Ben David Y., Warner E., Levitan M. et al. Autoimmune paraneoplastic cerebellar degeneration in ovarian carcinoma patients treated with plasmapheresis // Cancer. – 1996. – Vol. 78, № 10. – P. 2153-2156.

Bernard C.C.A., Johns T.G., Slavin A. et al. Myelin oligodendrocyte glycoprotein: a novel candidate autoantigen in multiple sclerosis // J. Mol. Med. - 1997. - Vol. 75, № 2. - P. 77-88.

Blaise S., Fiandrino G., Satger B., Carpentier P.H. [Lyme disease acrodermatitis chronica atrophicans: misleading vascular signs] // J. Mal. Vasc. (French) . – 2014. – Vol. 39, № 3. – P. 212-215.

Bonnan M., Valentino R., Olindo S. et al. Plasma exchange in severe spinal attacks associated with neuromyelitis optica spectrum disorder // Mult. Scler. – 2009. – Vol. 15, № 4. – P. 487-492.

Bonnan M., Cabre P. Plasma exchange in severe attacks of neuromyelitis optica // Mult. Scler. Int. – 2012. – 2012: 787630.

Boyette-Davis J.A., Walters E.T., Dougherty P.M. Mechanisms involved in the development of chemotherapy-induced neuropathy // Pain Manag. – 2015. – Vol. 5, № 4. – P. 285-296.

Brannagan Th.H., Nagle K.L., Lange D.J., Rowland L.P. Complications of intravenous immune globulin treatment in neurologic disease // Neurology. - 1996. - Vol. 47, № 3. - P. 674-677.

Brannagan T.H. Current treatments of chronic immune-mediated demyelinating polyneuropathies // Muscle Nerve. – 2009. – Vol. 39, № 5. – P. 563-578.

Brashear H.R., Phillips L.H. Autoantibodies to GABAergic neurons and response to plasmapheresis in stiff-man syndrome // Neurology. - 1991. - Vol. 41, № 10. - P. 1588-1592.

Burwinkel M., Riemer C., Schwartz A. et al. Role of cytokines and chemokines in prion infections of the central nervous system // Int. J. Dev. Neurosci. – 2004. – Vol. 22, № 7. – P. 497-505.

Buzzigoli S.B., Genovese M., Lambelet P. et al. Plasmapheresis treatment in Gillain-Barré syndrome: potential benefit over intravenous immunoglobulin // Anaesth. Intensive Care. – 2010. – Vol. 38, № 2. – P. 387-389.

Chiang L.M., Darras B.T., Kang P.B. Juvenile myasthenia gravis // Muscle. Nerve. – 2009. – Vol. 39, № 4. – P. 423-431.

Chiu H.C., Chen W.H., Yah J.H. Double filtration plasmapheresis in the treatment of inflammatory polyneyropathy // Ther. Apher. – 1997. – Vol. 1, № 2. – P. 183-186.

Clerico M., Rivorio C., Contessa G. et al. The therapy of multiple sclerosis with immune-modulating or immunosupressive drug. A critical evaluation based upon evidence based parameters and published systematic reviews // Clin. Neurol. Neurosirg. – 2008. – Vol. 110, № 9. – P. 878-886.

Clifford D.B., De Luca A., Simpson D.M. et al. Natalizumab-associated progressive multifocal leukoencephalopathy in patients with multiple sclerosis: lessons from 28 cases // Lancet Neurol. – 2010. – Vol. 9, № 4. – P. 438-446.

Chuang Y.C., Lee C.T., Chen J.B., Chee E.C. Experience in the treatment of myasthenia gravis with double filtration plasmapheresis // Chang Gung Med. J. – 2000. – Vol. 23, № 2. – P. 80-86.

Cortese I., Chaudhry V., So Y.T et al. Evidence-based guideline update: Plasmapheresis in neurologic disorders: Report of the Therapeutics and Technology Assessment Subcommitee of the American Academy of Neurology // Neurology. – 2011. – Vol. 76, №3. – P. 294-298.

Dada M.A., Kaplan A.A. Plasmapheres treatment in Guillain-Barré syndrome: potential benefit over IVIg in patients with axonal involvement // Ther. Apher. Dial. – 2004. – Vol. 8, № 5. – P.409-412.

Dalakas M.C. Basic aspects of neuroimmunology as they relate to immunotherapeutic targets: present and future prospects // Ann. Neurol. - 1995. - Vol. 37, Suppl. 1. - P. S2-S13.

Dau P.C., Denis E.H. Plasmapheresis and immunosupressive drug therapy in the Eaton-Lambert syndrome // Ann. Neurol. - 1982. - Vol. 11, № 6. - P. 570-575.

De Lau L.M., Siepman D.A., Remmers M.J. et al. Acute disseminating encephalomyelitis following legionnairs disease // Arch. Neurol. – 2010. – Vol. 67, № 5. – P.623-626.

Dhand U.K. Clinical approach to the weak patient in the intensive care unit // Respir. Care. – 2-1-. – Vol. 51, № 9. – P. 1024-1040.

Dick P.J., Low P.A., Windebank A.J. et al. Plasma exchange in polyneuropathy associated worth monoclonal gammapathy of undetermined significance // N. Eng. J. Med. - 1991. - Vol. 325, № 21. - P. 1482-1486.

Dick P.J., Litchy W.J., Kratz K.M. et al. A plasma exchange versus immune globulin infusion trial in chronic inflammatory demyelinating polyradiculoneuropathy // Ann. Neurol. - 1994. - Vol. 36, № 6. - P. 838-845.

Dropcho E.J. Autoimmune central nervous system paraneoplastic disorders: mechanisms, diagnosis, and therapeutic options // Ann. Neurol. - 1995. - Vol. 37, Suppl. 1. - P. S102-S113.

Boyette-Davis J.A., Walters E.T., Dougherty P.M. Mechanisms involved in the development of chemotherapy-induced neuropathy // Pain Manag. – 2015. – Vol. 5, № 4. – P. 285-296.

El-Bawab H., Hajjar W., Rafay M. et al. Plasmapheresis before thymectomy in myasthenia gravis: routine versus selective protocols // Eur. J. Cardiovasc. Surg. – 2009. – Vol. 35, № 3. – P. 392-397.

El-Bayoumi M.A., El-Rafaey A.M., Abdelkader A.M. et al. Comparison of intravenous immunoglobulin and plasma exchange in treatment of mechanically ventilated children with Guillain-Barré syndrome: a randomized study // Crit. Care. – 2011. – Vol. 15, № 4. – P. R164.

Fernandéz A.A., Martin A.P., Martinez M.I. et al. Cronic fatigue syndrome : aetiology, diagnosis and treatment // BMC Psychiatry. – 2009. – Vol. 9, Suppl 1. – P. S1.

Fleury M.C., Tranchant C. Myasthenia gravis // Rev. Prat. – 2008. – Vol. 58, № 20. – P. 2217-2224.

Fogan L. Progressive encephalomyelitis with rigidity responsive to plasmapheresis and immunosupression // Ann. Neurol. - 1996. - Vol. 40, № 4, -- P. 451-453.

Fukazawa T., Kikuchi S., Sasaki H. et al. Antinuclear antibodies and the optic-spinal form of multiple sclerosis // J. Neurol. - 1997. - Vol. 244, № 8. - P. 483-488.

Gaidos P., Chevret S., Clair B. et al. Clinical trial of plasma exchange and high-dose intravenous immunoglobulin in myasthenia Gravis // Ann. Neurol. - 1997. - Vol. 41, № 6. - P. 789-796.

Gambetti P., Parch P. Insomnia in prion diseases: sporadic and familial // New Engl. J. Med. - 1999. - Vol. 340, № 21. - P. 1675-1677.

Geschwind M.D., Tan KL.M., Lennon V.A. et al. Voltage-gated potassium channel autoimmunity mimicking Creutzfeldt-Jalob disease // Arch. Neurol. – 2008. – Vol. 65, № 10. – P. 1341-1346.

Gold R., Schneider-Gold C. Current and future standarts in treatment of myasthenia gravis // Neurotherapeutics. – 2008. – Vol. 5, № 4. – P. 535-541.

Gold R., Hohlfeld R., Toyka K.V. Progress in the treatment of myasthenia gravis // Ther. Adv. Neurol. Disord. – 2008. – Vol. 1, № 2. – P. 36-51.

Gorson K.C. An update on the management of chronic inflammatory demyelinating polyneuropathy // Ther. Adv. Neurol. Disord. – 2012. – Vol. 5, № 6. – P. 359-373.

Graf W.D., Katz J.S., Eder D.N. et al. Outcome in severe pediatric Guillain-Barré syndrome after immunotherapy or supportive care // Neurology. - 1994. - Vol, № 7. - P. 1494-1497.

Graus F., Vega F., Delatre J.Y. et al. Plasmapheresis and antineoplastic treatment CNS paraneoplastic syndrome with antineuronal autoantibodies // Neurology. - 1992. - Vol. 42, № 3. - P. 536-540.

Greenberg S.M., Hyman B.T. Cerebral amyloid angiopathy and apolipoptotein E: bad news to the good allele? // Ann. Neurol. - 1997. - Vol. 41, № 6. - P. 701-702.

Gwathmey K., Balogun R.A., Burns T. Neurologic indications for therapeutic plasma exchange: an apdate // J. Clin. Apher. – 2011. – Vol. 26, № 5. – P. 261-268.

Haditsch M., Kunze U. Tick-born encephalitis: a disease neglected by travel medicine // Travel Med. Infect. Dis. – 2-13. – Vol. 11, № 5. – P. 295-300.

Hagiwara H., Sakamoto S., Katsumata T., Katayama Y. Acute disseminated encephalomyelitis developed after Mycoplasma pneumoniae infection complicating subclinical measles infection // Intern. Med. – 2009. – Vol. 48, № 6. – P. 479-483.

Hanafusa N., Kondo Y., Suzuki M. et al. Double filtration plasmapheresis can decrease factor XIII activity // Ther. Apher. Dial. – 2007. – Vol.11, № 3. – P. 165-170.

Hao Q., Saida T., Yoshino H. et al. Anti-GalNAc-GD1a antibody-associated Guillain-Barré syndrome with a predominantly distal weakness without cranial nerve impairment and sensory disturbance // Ann. Neurol. – 1999. – Vol. 45, № 6. – P. 758-768.

Hashimoto H. Microscopic polyangiitis in systemic sclerosis // Int. J. Reumatol. – 2010, 2010: 148528.

Haupt W.F. Recent advances of therapeutic apheresis in Guillain-Barré syndrome // Ther. Apher. – 2000. – Vol. 4, № 4. – P. 271-274.

Hughes R.A., Wijdicks E.F., Barohn R. et al. Practice parameter: immunotherapy for Guillain-Barré syndrome: report of the Quality Standards Subcommittee of the American Academy of Neurology // Neurology. – 2003. – Vol. 61, № 6. – P. 736-740.

Hughes R.A., Swan A.V., Raphaël J.C. et al. Immunotherapy for Guillain-Barré syndrome: a systematic review // Brain. – 2007. – Vol. 130, Pt 9. – P. 2245-2257.

Hughes R.A.C. Give or take? Intravenous immunoglobulin or plasma exchange for Guillain-Barré syndrome // Crit. Care. – 2011. – Vol. 15, № 4. – P. 174.

Hund E.F., Fogel W., Krieger D. et al. Critical illness polyneuropathy: clinical findings and outcomes of a frequent cause of neuromuscular weaning failure // Crit. Car Med. – 1996. – Vol.24, № 8. – P. 1328-1333.

Iodice V., Kimpinski K., Vernini S. et al. Efficacy of immunotherapy in serpositive and seronegative putative autoimmune autonomic gangliopathy // Neurology. – 2009. – Vol. 72, № 23. – P. 2002-2008.

Jaben E.A., Pulido J.S., Pittick S. et al. The potential role of plasma exchange as treatment for bilateral diffuse uveal melanocytic proliferation: a report of two cases // J. Clin. Apher. – 2011. – Vol. 26, № 6. – P. 356-361.

Karim S., Majithia V. Devic's syndrome as initial presentation of systemic lupus erythematosus // Am. J. Med. Sci. – 2009. – Vol. 338, № 3. – P. 245-247.

Kaynar L., Altuntas F., Aydoglu I. et al. Therapeutic plasma exchange in patients with neurologic diseases: retrospective multicenter study // Transfus. Apher. Sci. – 2008. – Vol. 38, № 2. – P. 109-115.

Khatri B.O., McQuillen M.P., Hoffman R.G. Plasma exchange in chronic progressive multiple sclerosis. A long term study // Neurology. - 1991. - Vol. 41, № 4. - P. 409-414.

Khatri B.O., Man S., Giovannoni G. et al. Effect of plasma exchange in accelerating natalizumab clearance and restoring leukocyte function // Neurology. – 2009. – Vol. 72, № 5. – P. 402-409.

Kincaid J.C. Apheresis in treatment of the inflammatory demyelinating peripheral neuropathies // Ther. Apher. Dial. – 2002. – Vol. 6, № 1. – P. 53-56.

Koehler P.J., Kondstaal J. Lethal hypersensitivity myocarditis associated with the use of intravenous gammaglobulin for Guillain-Barré syndrome, in combination with phenitoin // Neurology. – 1996. – Vol. 243, № 4. – P. 366-367.

Köhler W., Bucka C., Klingel R. A randomized and controlled study comparing immunoadsorption and plasma exchange in myasthenic crisis // J. Clin. Apher.. – 2011. – Vol. 26, № 6. – P. 347-355.

Konishi T. [Plasmapheresis in patients with myasthenia gravis] // Nippon Rinsho. – 2008. – Vol. 66, № 6. – P. 1165-1171.

Kon'kova-Reidman A.B., Ratnikova L.I. [Neroimmune aspects of the pathogenesis and nitric oxide negative modifying the pathogenetic treatment of tick-borbe infections] // Zh. Nevrol. Psikhiatr. Im. S.S.Korsakova . – 2012. Vol. 112, № 2. – P. 40-45.

Kornberg A.J., Pertronk A. Chronic motor neuropathies: diagnosis, therapy, and pathogenesis // Ann. Neurol. - 1995. - Vol. 37, Suppl. 1. -S43-50.

Körner H., Riminton D.S., Stickland D.H. et al. Critical points of tumor necrosis factor action in central nervous system autoimmune inflammation defined by gene targeting // J. Exp. Med. - 1997. - Vol. 186, № 9. - P. - 1585-1590.

Keegan M., Pineda A.A., McClelland R.L. et al. Plasma exchange for severe attacks of CNS demyelination: predictors of response // Neurology. – 2002. – Vol. 58, № 1. – P. 143-146.

Landtblom A.M., Lindval B., Ledin T., Berlin G. A case report of plasmapheresis treatment in a patient with paraneoplastic cerebellar degeneration and high anti-yo antibody titres // Ther. Apher. Dial. – 2008. – Vol. 12, № 1. – P. 82-85.

Latov N. Pathogenesis and therapy of neuropathies associated with monoclonal gammapathy // Ann. Neurol. - 1995. - Vol. 37, Suppl. 1. - P. S32-42.

Levis R.A., Selwa J.F., Lisak R.P. Myasthenia gravis: immunological mechanisms and immunotherapy // Ann. Neurol. - 1995. - Vol. 37, Suppl. 1. - P. S51-S62.

Leys K., Lang B., Johnston I., Newsom-Davis J. Calcium channel autoantibodies in the Lambert-Eaton myasthenic syndrome // Ann. Neurol. - 1991. - Vol. 29, № 3. - P. 307-314.

Lin C.H., Jeng J.S., Yip P.K. Plasmapheresis in acute disseminated encephalomyelitis // J. Clin. Apher. – 2004. – Vol. 19, № 3. – P. 154-159.

Lindstrom J.M., Seybold M.E., Lenon V.A. et al. Antibody to acetylcholine receptor in myastenia gravis: prevalence, clinical correlates, and diagnostic value // Neurology. - 1998. - Vol. 51, № 4. - P. 933.

Liu J.F., Wang W.X., Xue J. et al. Comparing the autoantibody levels and clinical efficacy of double plasmapheresis, immunoadsorption, and intravenous immunoglobulin for the treatment of late-onset myasthenia gravis //Ther. Apher. Dial. – 2010. – Vol. 14, № 2. – P. 153-160.

Llufriu S., Castillo J., Blanco Y. et al. Plasma exchange for acute attacks of CNS demyelination: predictors of improvement at 6 months // Neurology. – 2009. – Vol. 73, № 12. – P. 949-953.

Lo Y.L. Clinical and immunological spectrum of the Miller Fisher syndrome // Muscle Nerve. – 2007. – Vol. 36, № 5. – P.615-627.

Lopate G., Parks B.J., Goldstein J.M. et al. Polyneuropathies associated with high titre antisulphatide antibodies: characteristics of patients with and without serum monoclonal proteins // J. Neurol. Neurosurg. Psychiatry. - 1997. - Vol. 62, № 6. - P. 581-585.

Lorusso L., Mikhailova S.V., Capelli E. et al. Immunological aspects of chronic fatigue syndrome // Autoiimun. Rev. – 2009. – Vol. 8, № 4. – P. 287-291.

Madrid A., Gil-Peralta A., Gil-Nécig E. et al. Morvan' s fibrillary chorea: remission after plasmapheresis // J. Neurol. - 1996. - Vol. 243, № 4. - P. 350-353.

Magaña S.M., Pittock S.J., Lennon V.A. et al. Neuromyelitis optica IgG serostatus in fulminant central nervous system inflammatory demyelinating disease // Arch. Neurol. – 2009. – Vol. 66, № 8. – P. 964-966.

Magaña S.M., Keegan B.M., Weinshenker B.G. et al. Beneficial plasma exchange response in CNS inflammatory demyelination // Arch. Neurol. – 2011. – Vol. 68, № 7. – P. 870-878.

Majorga C., Luque G., Romero F. et al. Antibodies to commercially available interferon-beta molecules in multiple sclerosis patients treated with natural interferon-beta // Int. Arch. Allergy Immunol. – 1999. – Vol. 118, № 2-4. – P. 368-371.

Mastriani J.A., Nixon R., Layzer R. et al. Prion protein conformation in patients with sporadic fatal insomnia // New Engl. J. Med. - 1999. - Vol. 340, № 21. - P. 1630-1638.

McDaneld L.M., Fields J.D., Bourdette D.N., Bhardwaj A. Immunomodulatory therapies in neurologic critical care // Neurocrit. Care. – 2010. – Vol. 12, № 1. – P. 132-143.

Meena A.K., Khadikar S.V., Murthy J.M.K. Teatment guidelines for Guillain-Barré syndrome // Ann. Indian Acad. Neurol. – 2011. – Vol. 14, Suppl. 1. – P.S73-S81.

Mirza M.K., Pogoriler J., Paral K. et al. Adjunct therapeutic plasma exchange for anti-N-methyl-D-aspartate receptor antibody encephalitis: a case report and review of literature // J. Clin. Apher. – 2011. – Vol. 26, № 6. – P. 362-365.

Misić-Majerus L., Bujić N., Madarić V., Avsić-Zupanc T. [Hepatitis caused by tick-borne meningoencephalitis virus (TBEV) – a rare clinical manifestation outside the central nervous system involvement] – Acta Med. Croatica (Croatian). – 2005. – Vol. 59, № 4. – P. 347-352.

Miyamoto K., Kusunoki S. Intermittent plasmapheresis prevents recurrence in neuromyelitis optica // Ther. Apher. Dial. – 2009. – Vol. 13, № 6. – P. 505-508.

Moll J.W.B., Hooijkaas H., van Goorbergh B.C.M. et al. Systemic and antineuronal autoantibodies in patients with paraneoplastic neurological disease // J. Neurol. - 1996. - Vol. 243, № 1. P. 51-56.

Myasthenia Gravis Clinical Group, Gajdos Ph., Chevret S. et al., Clinical trial of plasma exchenge and high-dose intravenous immunoglobulin im myasthenia gravis. – Ann. Neurol. – 1997. – Vol. 35, № 41. – P. 789-796.

Nachamkin I., Ung H., Moran A.P. et al. Ganglioside GM1 mimicry in *Campilobacter* strains from sporadic infections in the United States // J. Infect. Dis. – 1999. – Vol. 179, № 5. – P. 1183-1189.

Nakamura Y., Kawachi Y., Furuta J., Otsuka F. Sewere local skin reactions to interferon beta-1b in multiple sclerosis-improvement by deep subcutaneous injection // Eur. J. Dermatol. – 2008. – Vol. 18, № 5. – P. 579-582.

Netto A.B., Taly A.B., Kulkarni G.B. et al. Mortality in mechanically ventilated patients of Guillain-Barré syndrome // An. Indian Acad. Neurol. – 2011. – Vol. 14, № 4. – P. 262-268.

*Nordberg M., Forsberg P., Johansson A. et al.*Cytotoxic mechanisms may play a role in the local immune response in the central nervous system in neuroborreliosis // J. Neuroimmunol. – 2011. – Vol. 232, № 1-2. – P. 186-193.

Nowak R.J. Response of patients with refractory myasthenia gravis to rituximab: a retrospective study // Ther. Adv. Neurol. Disord. – 2011. – Vol. 4, № 5. – P. 259-266.

Offen D., Halevi S., Mosberg R. et al. Antibodies from ALS patients inhibit dopamine release mediated by L-type calcium channels // Neurology. - 1998. - Vol. 51, № 4. - P. 1100-1103.

Ohji S., Nomura K. [The indication of steroid therapy and apheresis therapy for multiple sclerosis] // Nippon. Rinsho. – 2008. – Vol. 66, № 6. – P. 1127-1132.

Okushin H., Morii K., Uesaka K., Yasa S. Twenty four-week peginterferon plus ribavirin after interferon-β induction for genotype 1b chronic hepatitis C // World J. Hepatol. – 2010. – Vol. 2, № 6. – P. 226-232.

Papazian O., Alfonso I. Juvenile myasthenia gravis // Medicina (B Aires). – 2009. – Vol. 69, № 1. – P. 71-83.

Park Y.-E., Yook J.-W., Kim D.-S. A case of Lewis-Sumner syndrome showing dramatic improvement after plasma exchange // J. Korean Med. Sci. – 2010. – Vol. 25, № 7. – P. 1101-1104.

Paulsen K.M., Pedersen B.N., Soleng A. et al. Prevalence of tick-born encephalitis virus in Ixodes ricinus ticks from three islands in north-western Norway // APMIS. – 2015. – Vol. 123, № 9. – P. 759-764.

Perera N.J., Lewis B., Tran H. et al. Refsum's disease-use of the intestinal lipase inhibitor, Orlistat, as novel therapeutic approach to a complex disorder // J. Obes. – 2011. – pii: 482021.

Pestronk A., Choki R. Multifocal motor neuropathy. Serum IgM anti-GM1 ganglioside antibodies in most patients detected using covalent lincage of Gm1 to ELISA plates // Neurology. - 1997. - Vol. 49, № 5. - P. 1289-1291.

Pham H.P., Daniel-Johnos J.A., Stotler B.A. et al. Therapeutic plasma exchange for the treatment of anti-NMDA receptor encephalitis // J. Clin. Apher. – 2011. – Vol. 26, № 6. – P. 320-325.

Pittayanon R., Treepraertsuk S., Phanthumchinda K. Plasmapheresis or intravenous immunoglobulin for myasthenia gravis crisis in King Chulalongkorn Memorial Hospital // J. Med. Assoc. Thai. – 2009. – Vol. 92, № 4. – P. 478-482.

Plasma Exchange / Sandoglobulin Gillain-Barré Syndrome Trial Group. Randomised trial of plasma exchange, intravenous immunoglobulin, and combined treatment in Guillain-Barré syndrome // Lancet. - 1997. - Vol. 349, № 9047. - P. 225-230.

Plosker D.L. Interferon-β-1b: a review of its use in multiple sclerosis // CNS Drugs. – 2011. – Vol. 25, № 1. – P. 67-88.

Pula J.H., MacDonald C.J. Current options for the treatment of optic neuritis // Clin. Opthalmol. – 2012. – № 6. – P. 1211-1223.

Rabie M., Nevo Y. Childhood acute and chronic immune-mediated polyradiculoneuropathies // Eur. J. Paediatr. Neurol. – 2009. – Vol. 13, № 3. – P. 209-218.

Rafael G.C., Chevret S. Rational therapy of Guillain-Barré syndrome // Lancet. - 1998. - Vol. 351, № 9104. -P. 753.

Ramesh G., Didier P.J., England J.D. et al. Inflammation in the pathogenesis of Lyme neuroborreliosis // Am. J. Pathol. – 2015. – Vol. 185, № 5. – P. 1344-1360.

Ramunni A., De Robertis F., Brescia P. et al. A case report of double filtration plasmapheresis in an acute episode of multiple sclerosis // Ther. Apher. Dial. – 2008. – Vol. 12, № 3. – P. 250-254.

Ric G.P.A., Paszner B., Oger J. et al. The evolution of neutralizing antibodies in multiple sclerosis patients treated with interferon β-1b // Neurology. – 1999. – Vol. 52, № 6. – P. 1277-1279.

Riemer C., Gültner S., Heise I. et al. Neuroinflammation in prion diseases: concepts and targets for therapeutic intervention // 2009. – Vol. 8, № 5. – P. 329-341.

Rogalewski A., Kraus J., Hasselblatt M. et al. Improvement of advanced postvaccinal demyelinating encephalitis due to plasmapheresis // Neuropsychiatr. Dis. Treat. – 2007. – Vol. 3, № 6. – P. 987-991.

Sanders D.B. Lambert-Eaton myasthenic syndrome: clinical diagnosis, immune-mediates mechanisms, and update on therapies // Ann. Neurol. - 1995. - Vol. 37, Suppl. 1. - P. S63-S73.

Sanford M., Lyseng-Williamson K.A. Subcutaneous recombinant interferon-β-1a (Rebif): a review of its use in the treatment of relapsing multiple sclerosis // Drugs. – 2011. – Vol. 71, № 14. – P. 1865-1891.

Saiz A., Arpa J., Sagasta A. et al. Autoantibodies to glutamic acid decarboxylase in three patients with cerebellar ataxia, late-onset insulin-dependent diabetes mellitus, and polyendocrine autoimmunity // Neurology. - 1997. - Vol. 49, № 4. - P. - 1026-1030.

Schimmel M., Bien C.G., Vincent A. et al. Successful treatment of anti-N-methyl-D-aspartate receptor encephalitis presenting with catatonia // Arch. Dis. Child. – 2009. – Vol. 94, № 4. – P 314-316.

Schröder A., Linker R.A., Gold R. // Plasmapheresis for neurologic disorders. – 2009. – Vol. 9, № 9. – P. 1331-1339.

Sevy A., Doche E., Squarcioni C. et al. Stroke in a young patient treated by alteplase heralding an acquired thrombotic thrombocytopenic purpura // J. Clin. Apher. – 2011. – Vol. 26, № 3. – P. 152-155.

Shariatmadar S., Noto T.A. Plasma exchange in stiff-man syndrome // Ther. Apher. – 2001. – Vol. 5, № 1. – P. 74-67.

Shinozaki K., Oda S., Sadahiro T. et al. A case report of plasmapheresis in the treatment of acute disseminated encephalomyelitis // Ther. Apher. Dial. – 2008. – Vol. 12, № 5. – P. 401-405.

Sinha S., Newsom-Devis J., Mills K. et al. Autoimmune aetiology for acquired neuromyotonia (Isaacs' syndrome) // Lancet. - 1991. - Vol. 338, № 8758. - P. 75-77.

Ramesh G., Didier P.J., England J.D. et al. Inflammation in the pathogenesis of Lyme neuroborreliosis // Am. J. Pathol. – 2015. – Vol. 185, № 5. – P. 1344-1360.

Smith R.G., Siklos L., Alexianu M.E. et al. Autoimmunity and ALS // Neurology. - 1996. - Vol. 47, № 4, Suppl. 2. - P. S40-S46.

Sorensen P.S. Neutralizing antibodies against interferon-beta // Ther. Adv. Neurol. Disord. – 2008. 0 Vol. 1, № 2. – P. 62-78.

Soria A., Maubec E., Henry-Feugeas M.C. et al. [Panniculitis induced by interferon beta-a] // Ann. Dermatol. Venerol. – 2007. – Vol. 134, № 4 Pt 1. – P. 374-377.

Sriram S., Rodrigues M. Indictment of the microglia as the villain in multiple sclerosis // Neurology. - 1997. - Vol. 48, № 2. - P. 464-470.

Staines D.R. Postulated vasoactive neurupeptide autoimmunity in fatigue-related conditions: a brief review and hypothesis // Clin. Dev. Imunol. – 2006. – Vol. 13, № 1. – P. 25-39.

Staines D.R. Is Parkinson's disease an autoimmune disorder of endogenous vasoactive neuropeptides? // Med. Hypotheses. – 2007. – Vol. 69, № 6. – P. 1208-1211.

Straub J., Chofflon M., Delavelle J. Early high-dose intravenous methylprednisolone in acute disseminated encephalomyelitis: A successful recovery // Neurology. - 1997. - Vol. 49, № 4. - P. 1145-1147.

Tan I.L., McArthur J.C., Clifford D.B. et al. Immune reconstitution inflammatory syndrome in natalizumab-associated PML // Neurology. – 2011. – Vol. 77, № 11. – P. 1061-1067.

Tanne D., D'Olhaberriague L., Schultz L.R. et al. Anticardiolipin antibodies and their associations with cerebrovascular risk factors // Neurology. – 1999. – Vol. 52, № 7. – P. 1368-1373.

Tharakan J., Jayapraksh P.A., Iyer V.P. Small volume plasma exchange in Guillain-Barre syndrome: experience in 25 patients // J. Assoc. Physicians India. – 1990. – Vol. 38, № 8. – P. 550-553.

The French Cooperative Group on Plasma Exchange in Guillain-Barré Syndrome. Appropriate number of plasma exchanges in Guillain-Barré Syndrome // Ann. Neurol. - 1997. - Vol. 41, № 3. - P. 299-306.

Tietjen G.E., Day M., Norris L. et al. Role of anticardiolipin antibodies in young persons with migraine and transient focal neurologic events // Neurology. - 1998. - Vol. 50, № 5. - P. 1433-1440.

Tranchant C. Therapeutic strategy in myasthenia gravis // Rev. Neurol. (Paris). – 2009. – V0l. 165, № 2. – P. 149-154.

Trebst C., Reising A., Kielstein J.T. et al. Plasma exchange therapy in steroid-unresponsive relapses in patients with multiple sclerosis // Blood Purif. – 2009. – V0l. 28, № 2. – P. 108-115.

Tuomi T., Björses P., Falorni A. et al. Antibodies to glutamic acid decarboxilase and insulin-dependent diabetes in patients with autoimmune polyendocrine syndrome typ I // J. Clin. Endocrin. Metab. - 1999. - Vol. 81, № 4. - P. 1488-1494.

Ueda T., Kanda F., Kobessho H. et al. “Droped head syndrome” caused by Lambert-Eaton myasthenic syndrome // Muscle Nerve. – 2009. – Vol. 40, № 1. – P. 134-136.

Valbonesi M., Bo A., De Luidgi M.C. et al. Cascade filtration (CF) with the Haemonetics MCS+: a new technical adaptation // Int. J. Artif. Organs. – 2001. – Vol. 24, № 3. – P. 164-166.

Van Boxel-Dezaire A.H.H., Hoff S.C.J., van Oosten B.W. et al. Decreased interleukin-10 and increased interleukin-12p40 mPNA are associated with disease activity and characterize different discase stages in miltiple sclerosis // Ann. Neurol. – 1999. – Vol. 45, № 6. – P. 695-703.

Wanders R.J.A., Waterham H.R., Leroy B.P. Refsum disease / In: Pagon R.A. editors. GeneReviews [Internet}. Seattle (WA): University of Washington, Seattle; 1993-2006 [updated 2010- Apr. 22].

Wang K.C., Wang S.J., Lee C.L. et al. The rescue effect of plasma exchange for neuromyelitis optica // J. Clin. Neurosci. – 2011. – Vol. 18, № 1. – 43-46.

Watanabe S., Nakashima I., Misu T. et al. Therapeutic efficacy of plasma exchange in NMO-IgG-positive patients with neuromyelitis optica // Mult. Scler. – 2007. – Vol. 13, № 1. – P. 128-132.

Weinshenker B.G. Plasma exchange for acute attacks of demyelinating disease: detecting a Lazarus effect // Ther. Apher. – 2000. – Vol 4, № 3. – P. 187-189.

Widhe M., Grussell M., Ekerfelt C. et al. Cytokines in Lyme borreliosis: lack of early tumor necrosis factor-α and transforming growth factor-β_1 responses are associated with chronic neuroborreliosis // Immunology. – 2002. – Vol. 107, № 1. – P. 46-55.

Widhe M., Jarefors S., Ekerfelt C. et al. Borrelia-specific interferon-gamma and interleukin-4 secretion in cerebrospinal fluid and blood during Lyme borreliosis in humans: association with clinical outcome // J. Infect. Dis. – 2004. – Vol. 189, № 10. – P. 188-191.

Winters J.L., Brown D., Hazard E. et al. Cost-minimization analysis of the direct costs of TPE and IVIg in the treatment of Guillain-Barré syndrome // BMC Health. Serv. Res. – 2011. – № 11. – P. 101.

Yeh J.H., Chiu H.C. Comparison between double-filtration plasmapheresis and immunoadsorption plasmapheresis in the treatment of patients with myasthenia gravis // J. Neurol. – 2000. – Vol. 247, № 7. – P. 510-513.

Yeh J.H., Chen W.H., Chiu H.C. Double filtration plasmapheresis in the treatment of myasthenic crisis – analysis of prognostic factors and efficacy // Acta Neurol. Scand. – 2001. – Vol. 104, № 2. – P. 78-82.

Yeh J.H., Chen W.H., Chiu H.C. Predicting the course of myasthenic weakness following double failtration plasmapheresis // Acta Neurol. Scand. – 2003. – Vol. 108, № 3. – P. 174-178.

Yeh J.H., Chen W.H., Huang K.M., Chiu H.C. Prethymectomy plasmapheresis in myasthenia gravis // J. Clin. Apher. – 2005. - Vol. 20, № 4. – P. 217-221.

*Yin Z., Braun J., Neure L. et al.*T cell cytokine pattern in the joints of patients with Lyme arthritis and its regulation by cytokines and anticytokines // Arthritis Reum. – 1997. – Vol. 40, № 1. – P. 69-79.

Yoshida H., Ando A., Sho K. et al. Anti-aquaporin-4 antibody-positive optic neuritis with double-filtration plasmapheresis // J. Ocul. Pharmacol. Ther. – 2010. – Vol. 26, № 4. – P. 381-385.

Yücesan C., Arslan O., Arat M. et al. Therapeutic plasma exchange in the treatment of neuroimmunologic disorders: review of 50 cases // Transfus. Apher. Sci. – 2008. Vol. 36, № 1. – P. 103-107.

Yuki N., Tagawa Y., Handa S. Autoantibodies to peripheral nerve glycosphingolipids SPG, SLPG, and SGPG in Guillain-Barré syndrome and chronic inflammatory demyelinating polyneuropathy // J. Neuroimmunol. - 1996. - V. 70, № 1. - P. 1-6.

Yuki N., Koda M., Hirata K. Isolated internal ophthalmoplegia associated with immunoglobulin G anti-GQ1b antibody // Neurology. – 1998. – Vol. 51, № 5. – P. 1515-1516.

Yuki N. Fisher syndrome and Bickerstaff brainstem encephalitis (Fisher-Bickerstaff syndrome) // J. Neuroimmunol. – 2009. – Vol. 215, № 1-2. – P. 1-9.

Zarkou S., Carter J.L., Wellik K.E. et al. Are corticosteroids efficacious for preventing or treating neutralizing antibodies in multiple sclerosis patients treated with beta-interferons? A critically appraised topic // Neurologist. – 2010. – Vol. 16, № 3. – P. 212-214.

Zisimopoulou P., Lagoumintzis G., Kostelidou K. et al. Towards antigen-specific apheresis of pathogenic autoantibodies as a further step in the treatment of myasthenia gravis by plasmapheresis // J. Neuroimmunol. – 2008. – Vol. 15, 201-202. – P. 95-103.

Russian literature

Barbas I.M., Skoromets A.A. [Multiple Sclerosis. Experience in the treatment and prevetion of exacerbations]. – Saint-Petersburg.: SOTIS, 2003. – 123 p.

Cherny V.I., Shramenko E.K., Logvinenko L.V. et al. [Plasmapheresis for complex treating of demyelinating nervous diseases] // Medico-social problems of family. – 2004. – Vol. 9, № 2. – P. 29-33.

Evdokimov A.V., Gerasimov M.M. [Clinico-immunological comparison at the end of cerebral stroke] // Allergology Immunology. – 2006. – Vol. 7, № 3. – P. 419-420.

Elchaninov A.P., Gendel L.L., Belenky L.M. et al. [Efferent therapy for complex treating of patients during acute period of ischemic stroke in association with lupus anticoagulant (primary antiphospholipid syndrome)] // Efferent Therapy. – 2003. – Vol.9, № 1. – P. 80-81.

Elchaninov A.P., Gendel L.L., Belenky L.M. [Efferent therapy for complex treating of patients with discirculation encephalopathy associated with lupus anticoagulant (primary antiphospholipid syndrome)] // Efferent Therapy. – 2003. – Vol. 9, № 1. – P. 81-82.

Fomina L.A., Gerasimova M.M. [Clinico-immunological analysis on discirculation in vertebro-basilar system] // Allergology Immunology. – 2006. – Vol. 7, № 3. – P. 420.

Kosachev V.D., Yulev N.M., Bechik S.L. [Plasma exchange for complex treating of myasthenia] // Efferent Therapy. – 2006. – Vol. 12, № 2. – P. 28-31.

Marchuk A.I., Bulanova N.M. [Cupping of migraine attacks with the help of therapeutic apheresis] // Proc. IX Confer. Moscow hemapheresis society. - Moscow., 1999. - P. 32.

Orlova Yu.Yu. [Immunological and biochemical parallels of various types course of multiple sclerosis]: Author's abstract magister dissertation. - Novosibirsk, 1999. - 22 p.

Popova L.M. [Amyotrophic lateral sclerosis in prolonged life]. - Moscow: Medicine, 1998. - 143 p.

Shapoval A.N. [Tick-born encephalitis]. – Moscow: Medicine, 1980. - 252 p.

Voinov V.A. [Efferent therapy. Membrane plasmapheresis]. – M., 2010. – 400 p.

Vostrikova I.L., Kimova M.V., Ponomarenko H.A. et al. [Specificity of antibody mediated proteolysis of myelin basic protein in multiple sclerosis: pathogenetic and clinical aspects] // Allergology Immunology. – 2006. – Vol. 7, № 3. – P. 414.