Eur Arch Psychiatry Clin Neurosci (1992) 242:122–126

European Archives of Psychiatry and Clinical Neuroscience

Are CSF or Serum Ganglioside Antibodies Related to Peripheral Nerve Demyelination in Neuroborreliosis, Guillain-Barré Syndrome, or Chronic Inflammatory Demyelinating Polyradiculoneuropathy?*

Michael Weller, Andreas Stevens, Norbert Sommer, and Horst Wiethölter

Neurologische Klinik der Universität Tübingen

Received September 9, 1992

Summary. Cerebrospinal fluid (CSF) and serum IgG and IgM antibodies to seven gangliosides were determined in patients with neuroborreliosis (NB) ($n = 20$), Guillain-Barré syndrome (GBS) ($n = 13$), and chronic inflammatory demyelinating polyradiculoneuropathy (CIDP) ($n = 10$). The incidence of elevated antibodies was highest in NB and lowest in CIDP. Correlation between CSF and serum antibodies was only observed for IgG antibodies to GM1, GD1b and GT1b in GBS. The strong IgM antibody reactivity to gangliosides in the CSF of NB patients may be involved in the variety of neurological disorders attributed to *Borrelia burgdorferi* infection. Since one CIDP and three GBS patients had serologic evidence of prior or concurrent borrelia infection, this infection may belong to the infections that can trigger GBS or CIDP. The lack of specific ganglioside antibody patterns in these four patients suggests that ganglioside antibodies are not the link between *Borrelia burgdorferi* infection and the demyelination of peripheral nerves in GBS and CIDP.

Key words: Ganglioside antibodies – CSF – Neuroborreliosis – GBS – CIDP

Introduction

Infection with the spirochete, *Borrelia burgdorferi*, has been associated with a variety of neurological disorders including the classical meningopolyradiculomyelitis of Garin-Bujadoux and Bannwarth (Hörstrup and Ackermann 1973; Ackermann 1976; Kristoferitsch et al. 1983; Pfister et al. 1984; Pachner et al. 1985; Schmidt and Ackermann 1985), encephalopathy (Halperin et al. 1989, Pachner et al. 1989), motor neuron disease (Halperin et al. 1990), and Guillian-Barré syndrome (GBS) (Bouma et al. 1989; Mancardi et al. 1989; López de Munain et al. 1990). Some neurological complications of borreliosis have been attributed to autoimmune mechanisms triggered by the infection (Sigal and Tatum 1988; Pachner et al. 1989). Since the putative autoimmune etiology of GBS includes serum antibodies to gangliosides (Ilyas et al. 1988, 1991, 1992a, b; Gregson et al. 1991; Van den Berg et al. 1992), we have studied the incidence of elevated antibodies to several gangliosides in the cerebrospinal fluid (CSF) and serum of patients with typical neuroborreliosis (NB) (meningopolyradiculomyelitis Garin-Bujadoux-Bannwarth), as well as patients with GBS or chronic inflammatory demyelinating polyradiculoneuropathy (CIDP). Specifically, we sought to identify autoimmune phenomena in NB and tested the hypothesis that ganglioside antibodies are responsible for the partial clinical overlap between NB, GBS und CIDP.

Material and Methods

We studied CSF and serum samples of patients with NB ($n = 20$), GBS ($n = 13$), and CIDP ($n = 10$), who were diagnosed and treated at the University Department of Neurology, Tübingen, Germany. The diagnosis of NB was established as previously described (Weller et al. 1991b). The NB patients included in this study represent the typical type of acute neuroborreliosis Garin-Bujadoux-Bannwarth: all patients had cervicobrachial or thoracolumbar polyradiculoneuritic syndromes of acute onset, 6 had a peripheral facial nerve palsy. In addition to this classical clinical presentation, detection of specific CSF and serum antibodies to *Borrelia burgdorferi*, performed at the Max von Pettenkofer Institute, Munich, Germany (Wilske et al. 1986), was required to be included in this study. GBS and CIDP patients fulfilled standard diagnostic criteria

* Some results reported in this study have been presented at the Second Congress of the Pan-European Society of Neurology in Vienna, Austria, December 1991.

Correspondence to: Prof. Dr. H. Wiethölter, Bürgerhospital, Neurologische Klinik, Tunzhofer Straße 14–16, W-7000 Stuttgart 1, Federal Republic of Germany

(Asbury et al. 1978; Barohn et al. 1989). The CSF and blood samples were obtained prior to antimicrobial or antiinflammatory pharmacotherapy. The time interval between the onset of symptoms and the lumbar punctures in the NB patients varied between 4 and 19 days.

Total CSF and serum IgM and IgG and the presence of oligoclonal bands on isoelectric focusing gels were determined as previously described (Weller et al. 1991a, b). Antibodies to gangliosides GM1, GM2, GM3, AGM1, GD1a, GD1b, and GT1b (Sigma, St. Louis, MO, USA) in CSF and serum were determined by enzyme-linked immunoadsorbent assay (ELISA) according to modified standard procedures (Marcus et al. 1989; Weller et al. in press, Stevens et al. in press). Correlation of the ELISA findings with ganglioside antigen recognition on thin layer chromatography of purified ganglioside antigens (Sigma, St. Louis, MO, USA) served as a control for assay specificity.

Serum samples were diluted 1:50 in phosphate-buffered saline (PBS) for the ELISA assay. Initially, we used a standardized CSF dilution of 1:5 in PBS. This approach was later discontinued since there was an obvious effect of the total amount of immunoglobulin in the CSF on the optical density (OD) readings, possibly indicating an increased non-specific binding in samples with increased IgG or IgM. This made a comparison between different patients and different disorders very difficult. Although a standardized CSF dilution compares the actual in vivo biochemistry better than any normalized dilution and reflects the real amount of putatively damaging antibodies in the subarachnoid space, it does not contribute to a differentiation of plasma exudation versus intrathecal immunoglobulin synthesis. Since blood-brain barrier dysfunction is a hallmark of GBS, CIDP, and NB, we then decided to adjust the CSF to an IgG concentration of 5 mg/l in PBS to estimate the relative amount of ganglioside reactive antibodies in the CSF. A similar adjustment was not necessary for the serum samples since serum IgG and IgM did not differ between the three disorders and controls. This approach will help to identify differences between CSF and serum antibodies and may indicate intrathecal immunoglobulin synthesis.

An alternative and possibly even superior approach not pursued in this study would have been a normalization according to the ratios of CSF versus serum albumin as an indicator of blood brain barrier dysfunction. In the case of NB, GBS, and CIDP, the approaches of normalizing CSF IgG or CSF/serum albumin ratios yield very similar results since the contribution of intrathecal IgG synthesis to total CSF IgG according to Reiber and Felgenhauer (1987) has been estimated to be only 16% in NB, 0% in GBS, and 4% in CIDP (Weller et al. 1991b). The results provided below and in the tables are those obtained after normalization of CSF IgG to 5 mg/l.

The samples were incubated in triplicate for 24 hours at 4°C in micro-ELISA plates (M129A Dynatech, Denkendorf, Germany) precoated with purified ganglioside antigen (150 ng/well) dissolved in pure methanol and evaporated at room temperature. Protein binding sites in the plastic wells were blocked by 0.1% bovine serum albumin in PBS prior to the incubation of CSF or serum samples. IgG and IgM ganglioside antibodies bound to the ELISA plate were labeled using anti-human IgG (Sigma A-5403) and anti-human IgM (Sigma A-3914) alkaline phosphatase (AP) conjugate diluted 1:1000 in PBS. AP activity was measured colorimetrically by conversion of p-nitrophenyl phosphate in an automated ELISA reader (Flow, Meckenheim, Germany). Differentiation of monoclonal and polyclonal IgM antibodies was performed as previously outlined (Weller et al. in press).

Seven internal controls were included in each run. These were either serum samples from healthy volunteers or CSF samples from patients with suspected but eventually disproven neurological disease. We calculated normalized OD readings defined as ratios of patient OD over the mean OD of the seven internal controls. Elevated OD readings were defined as OD readings above the confidence interval for $P < 0.03$. The data obtained from the NB, GBS, and CIDP patients were compared with a control group of patients ($n = 24$) with other non-inflammatory neurological diseases including normal pressure hydrocephalus ($n = 6$), senile dementia ($n = 5$), or with suspected but eventually disproven neurological disease ($n = 13$). Ganglioside antibodies in these 24 patients did not differ from the above-mentioned seven internal controls. Statistical analysis included ANOVA and multiple linear correlation analysis.

Results

The normalized OD readings for CSF ganglioside antibodies in the three disorders and in the control group are presented in Table 1. The incidence of elevated CSF and serum antibodies is given in Table 2. All elevated IgM

Table 1. Mean CSF IgG and IgM normalized OD readings and standard error of the mean (SEM) to seven gangliosides in NB, CBS, CIDP and in controls

	NB ($n = 20$)	GBS ($n = 13$)	CIDP ($n = 10$)	Controls ($n = 24$)
GM1 IgG	1.10 ± 0.04	1.46 ± 0.20[a]	0.98 ± 0.07	1.00 ± 0.15
GM1 IgM	1.25 ± 0.07[a, c]	1.13 ± 0.04[a, d]	1.03 ± 0.04	1.06 ± 0.15
GM2 IgG	1.04 ± 0.04	1.03 ± 0.04	1.02 ± 0.08	1.04 ± 0.11
GM2 IgM	1.39 ± 0.04[a, c]	1.14 ± 0.05[a]	1.04 ± 0.03	1.00 ± 0.14
GM3 IgG	1.21 ± 0.04[a]	1.34 ± 0.07[a]	1.21 ± 0.08	1.00 ± 0.11
GM3 IgM	1.56 ± 0.07[a, c]	1.32 ± 0.09[a]	1.09 ± 0.06	1.00 ± 0.11
AGM1 IgG	1.17 ± 0.05[a]	1.30 ± 0.21[a]	1.10 ± 0.06	0.99 ± 0.14
AGM1 IgM	1.21 ± 0.05[a, c]	1.00 ± 0.01	1.05 ± 0.03	0.99 ± 0.06
GD1a IgG	1.19 ± 0.04[a]	1.00 ± 0.03	1.05 ± 0.08	1.01 ± 0.12
GD1a IgM	1.35 ± 0.06[a–c]	1.02 ± 0.03	0.94 ± 0.04	0.98 ± 0.08
GD1b IgG	1.12 ± 0.03	1.00 ± 0.05	1.06 ± 0.07	1.00 ± 0.12
GD1b IgM	1.24 ± 0.05[a, c]	1.10 ± 0.02[a]	1.03 ± 0.03	1.00 ± 0.06
GT1b IgG	1.07 ± 0.04	1.14 ± 0.04[a]	1.18 ± 0.07[a]	1.00 ± 0.13
GT1b IgM	1.29 ± 0.05[a–c]	1.10 ± 0.04	1.13 ± 0.04[a]	1.00 ± 0.10

[a] Indicates a significant difference between any of the three disorders and controls,
[b] between NB and GBS,
[c] between NB and CIDP, and
[d] between GBS and CIDP

Table 2. Incidence of elevated IgG and IgM ganglioside antibodies in CSF and serum of NB ($n = 20$), GBS ($n = 13$), and CIDP ($n = 10$) patients

	NB		GBS		CIDP	
	CSF	Serum	CSF	Serum	CSF	Serum
GM1 IgG	4	3	5	2	2	1
GM1 IgM	5	2	3	0	0	2
GM2 IgG	7	3	0	0	1	1
GM2 IgM	5	1	4	0	0	1
GM3 IgG	11	4	8	0	3	3
GM3 IgM	16	2	7	1	2	1
AGM1 IgG	4	1	3	2	1	1
AGM1 IgM	14	2	0	0	0	1
GD1a IgG	14	3	0	1	1	1
GD1a IgM	14	1	2	0	0	1
GD1b IgG	7	2	1	2	1	3
GD1b IgM	6	2	0	1	0	1
GT1b IgG	2	2	2	1	3	1
GT1b IgM	8	3	2	0	2	1

Table 3. Clinical and laboratory data in four patients seropositive for *Borrelia burgdorferi* infection. All patients had pathological specific serum IgG titres, one (Patient 2) had an increased IgM titre, on admission. There were no specific antibody titres and no oligoclonal immunoglobulin bands detectable in the CSF

Age gender	Clinical diagnosis	CSF cells per mm^3	CSF IgG mg/l	CSF Alb. mg/l	Serum IgG g/l	Serum Alb. g/l	IgG Index
54 m	GBS	2	95	619	10.2	40.3	0.61
36 m	GBS	4	75	343	14.1	39.5	0.61
62 m	GBS	7	535	2030	16.9	48.1	0.77
75 m	CIDP	27	246	1020	15.5	38.5	0.59

OD readings were of polyclonal origin. When NB, GBS, and CIDP patients were pooled ($n = 43$), CSF IgG and IgM antibodies to GM3 (22/43, 51%, and 26/43, 60%) were elevated most often. Elevated IgG to GD1a and elevated IgM to GM3, AGM1, and GD1a were very common in NB (Table 2). Of the total of 14 ganglioside antibody OD readings, 7 IgG and 7 IgM readings, 10 were elevated in NB, 8 in GBS, and 2 in CIDP. The three disorders could not be distinguished by the elevation of different CSF IgG antibodies (Table 1). NB patients had higher CSF IgM readings than CIDP patients to all gangliosides. Compared to GBS, IgM OD readings in NB were only higher to GD1a and GT1b. IgM antibodies in GBS and CIDP differed only for GM1.

A comparison of serum ganglioside antibodies among NB, GBS, and CIDP patients did not yield remarkable findings. ANOVA revealed lower IgG anti-GM3 in GBS than in either NB or CIDP. CIDP patients had higher IgG anti-AGM1 than NB patients, and NB patients had higher IgM anti-GD1b than GBS patients. A correlation analysis of CSF and serum antibodies revealed positive correlation for IgG antibodies to GM1 ($r = 0.90$, $P = 0.0024$), GD1b ($r = 0.81$, $P = 0.015$), and GT1b ($r = 0.77$, $P = 0.023$) in GBS. There was no such correlation in NB or CIDP. One CIDP and three GBS patients had serologic evidence of *Borrelia burgdorferi* infection (Table 3). None of them had specific intrathecal antibody formation. No specific pattern of CSF or serum ganglioside antibodies was observed in these patients.

Discussion

Serum ganglioside antibodies have been described in a plethora of neurological and non-neurological disorders in the recent years (Sadiq et al. 1990; Adams et al. 1991; Weller et al. in press). Very little is known about the occurrence and a pathogenetic significance of these antibodies in the CSF.

The present work compares the CSF and serum ganglioside antibody pattern of NB, GBS, and CIDP patients. The detection of serum ganglioside antibodies in NB patients confirms the suggestion that antibodies induced by infection with *Borrelia burgdorferi* may cross-react with nervous system antigens (Sigal and Tatum 1988). Prior reports (Ryberg et al. 1984; Vedeler et al. 1988) had failed to detect antibodies to total brain lipid antigen or brain or nerve root homogenate in NB although such reactivity was found in GBS. The antibody reactivity in NB is predominantly of CSF and IgM origin (Tables 1, 2) and corresponds to the strong intrathecal IgM response in NB previously characterized (Maida et al. 1986; Weller et al. 1991b).

It is possible that a remote or recent *Borrelia burgdorferi* infection was an etiology or a predisposing factor in four of twentythree patients with GBS or CIDP in this study. We suggest that this infection be included among the putative etiologies of GBS and CIDP. We would recommend to give these patients an appropriate course of antimicrobial treatment early in the course of their disease, despite the fact that there are currently no clinical data available to support this strategy.

Antibodies to peripheral nerve antigens are thought to mediate peripheral demyelination in GBS and CIDP (Koski et al. 1985; Ilyas et al. 1988). We tested and have to reject the hypothesis that two putative clinical manifestations of *Borrelia burgdorferi* infection, GBS and CIDP, are related to the formation of ganglioside antibodies. Similarly, the association between GBS after infection with *Campylobacter jejuni* and serum antibodies to GM1 has remained controversial (Yuki et al. 1990; Van der Meché et al. 1991; Walsh et al. 1991) In the present study, polyclonal IgG and IgM antibodies to gangliosides were as frequent in NB patients suffering from typical meningopolyradiculomyelitis as they were in those seropositive patients suffering from GBS or CIDP. Further, the seropositive CIDP and GBS patients did not differ from seronegative CIDP or GBS patients in their CSF or serum IgG or IgM antibody reactivity to gangliosides. There was no correlation between CSF and serum antibodies except for IgG antibodies to GM1, GD1b and GT1b in GBS. The latter finding may be ac-

counted for by blood-brain barrier dysfunction in GBS. The lack of correlation between CSF and serum antibody elevation in most instances provides evidence against CSF antibodies being solely derived from exudation across a disturbed blood brain barrier. The probable intrathecal ganglioside antibody synthesis corresponds to the high incidence of oligoclonal immunoglobulin detection on CSF isoelectric focusing gels in NB (Weller et al. 1991b). However, since conventional isoelectric focusing methods are suitable for oligoclonal IgG but not IgM detection (Sharief et al. 1989), the ganglioside antibody reactivity which is predominantly of IgM type would not necessarily have to be associated with the detection of oligoclonal bands.

In summary, we have detected antibody reactivity with multiple gangliosides in the CSF of NB patients which may represent cross-reactive antibodies induced by spirochetal antigens and which may contribute to the widespread nervous system pathology associated with NB. Our results suggest that the clinical overlap of NB, GBS, and CIDP, peripheral nerve demyelination, is not caused by ganglioside antibodies.

References

Ackermann R (1976) Durch Zecken übertragene Meningopolyneuritis (Garin-Bujadoux, Bannwarth). Münch Med Wochenschr 118:1621–1622

Adams D, Kuntzer T, Burger D, Chofflon M, Magistris MR, Regli F, Steck AJ (1991) Predictive value of anti-GM1 ganglioside antibodies in neuromuscular disease. J Neuroimmunol 32:223–230

Asbury AK, Arnason BG, Karp HR, McFarlin DE (1978) Criteria for diagnosis of Guillain-Barré syndrome. Ann Neurol 3:565–566

Barohn RJ, Kissel JT, Warmolts JR, Mendell JR (1989) Chronic inflammatory demyelinating polyradiculoneuropathy. Clinical characteristics, course and recommendations for diagnostic criteria. Arch Neurol 46:878–884

Bouma PAD, Carpay HA, Rijpkema SGT (1989) Antibodies to Borrelia burgdorferi in Guillain-Barré syndrome. Lancet ii: 739

Gregson NA, Jones D, Thomas PK, Willison HJ (1991) Acute motor neuropathy with antibodies to GM1 ganglioside. J Neurol 238:447–451

Halperin JJ, Luft BJ, Anand AK, Roque CT, Alvarez O, Volkman DJ, Dattwyler RJ (1989) Lyme neuroborreliosis: central nervous system manifestations. Neurology 39:753–759

Halperin JJ, Kaplan GP, Branzinsky S, Tsai TF, Cheng T, Ironside A, Wu P, Delfiner J, Golightly M, Brown RH, Dattwyler RJ, Luft BJ (1990) Immunologic reactivity against Borrelia burgdorferi in patients with motor neuron disease. Arch Neurol 47:586–594

Hörstrup P, Ackermann R (1973) Durch Zecken übertragene Meningopolyneuritis (Garin-Bujadoux, Bannwarth). Fortschr Neurol Psychiatr Grenzgeb 41:583–606

Ilyas AA, Willison HJ, Quarles RH, Jungalwala FB, Cornblath DR, Trapp BD, Griffin DE, Griffin JW, McKhann GM (1988) Serum antibodies to gangliosides in Guillain-Barré syndrome. Ann Neurol 23:440–447

Ilyas AA, Mithen FA, Chen ZW, Cook SD (1991) Search for antibodies to neutral glycolipids in sera of patients with Guillain-Barré syndrome. J Neurol Sci 102:67–75

Ilyas AA, Mithen FA, Chen ZW, Cook SD (1992a) Anti-GM1 IgA antibodies in Guillain-Barré syndrome. J Neurol Sci 106:69–76

Ilyas AA, Mithen FA, Dalakas MC, Chen ZW, Cook SD (1992b) Antibodies to acidic glycolipids in Guillain-Barré syndrome and chronic inflammatory demyelinating polyneuropathy. J Neurol Sci 107:111–121

Koski CL, Humphrey R, Shin ML (1985) Anti-peripheral myelin antibody in patients with demyelinating neuropathy: quantitative and kinetic determination of serum antibody by complement component 1 fixation. Proc Natl Acad Sci USA 82:905–909

Kristoferitsch W, Spiel G, Wessely P (1983) Zur Meningopolyneuritis (Garin-Bujadoux, Bannwarth). Klinik und Laborbefunde. Nervenarzt 54:640–646

López de Munain A, Espinal Valencia JB, Martí-Massó JF, Pérez-Trallero E, García-Arenzana JM (1990) Antibodies to Borrelia burgdorferi in Guillain-Barré syndrome. Lancet 335:1168

Maida E, Kristoferitsch W, Spiel G (1986) Liquorveränderungen bei Meningoradiculitits Garin-Bujadoux-Bannwarth. Nervenarzt 57:149–152

Mancardi GL, Del Sette M, Primavera A, Farinelli M, Fumarola D (1989) Matters arising. A prospective study of acute idiopathic neuropathy. II Antecedent events. J Neurol Neurosurg Psychiatry 52:424–425

Marcus DM, Latov N, Hsi BP, Gillard BK, and participating laboratories (1989) Measurement and significance of antibodies against GM1 ganglioside. J Neuroimmunol 25:255–259

Pachner A, Steere AC (1985) The triad of neurological manifestations of Lyme disease: meningitis, cranial neuritis, and radiculoneuritis. Neurology 35:47–53

Pachner A, Duray P, Steere AC (1989) Central nervous system manifestations of Lyme disease. Arch Neurol 46:790–795

Pfister HW, Einhäupl K, Preac-Mursic V, Wilske B, Schierz G (1984) The spirochetal etiology of lymphocytic meningoradiculitis of Bannwarth (Bannwarth's syndrome). J Neurol 231: 141–144

Reiber H, Felgenhauer K (1987) Protein transfer at the blood cerebrospinal fluid barrier and the quantitation of the humoral immune response within the central nervous system. Clin Chim Acta 163:319–328

Ryberg B, Hindfelt B, Nilsson B, Olsson JE (1984) Anti-neural antibodies in Guillain-Barré syndrome and lymphocytic meningoradiculitis (Bannwarth's syndrome). Arch Neurol 41:1277–1281

Sadiq SA, Thomas FP, Kilidereas K, Protopsaltis S, Hays AP, Lee KW, Romas SN, Kumar N, Van den Berg L, Santoro M, Lange DJ, Younger DS, Lovelace RE, Trojaborg W, Sherman WH, Miller JR, Minuk J, Fehr MA, Roelofs RI, Hollander D, Nichols III FT, Mitsumoto H, Kelley JJ, Swift TR, Munsat TL, Latov N (1990) The spectrum of neurologic disease associated with anti-GM1 antibodies. Neurology 40:1067–1072

Schmidt R, Ackermann R (1985) Durch Zecken übertragene Meningo-Polyneuritis (Garin-Bujadoux, Bannwarth). Erythema-chronicum-migrans-Krankheit des Nervensystems. Fortschr Neurol Psychiatr 53:145–153

Sharief MK, Keir G, Thompson EJ (1989) Glutaraldehyde-enhanced immunofixation: a sensitive new method for detecting oligoclonal IgM. J Neuroimmunol 23:149–156

Sigal LH, Tatum AH (1988) Lyme disease patients' serum contains IgM antibodies to Borrelia Burgdorferi that cross-react with neuronal antigens. Neurology 38:1439–1442

Stevens A, Weller M, Wiethölter H (1992) Differing CSF and serum antibodies in chronic progressive and relapsing remitting multiple sclerosis. Acta Neurol Scand in press

Van den Berg LH, Marrink J, De Jager AEJ, De Jong HJ, Van Imhoff GW, Latov N, Sadiq SA (1992) Anti-GM1 antibodies in patients with Guillain-Barré syndrome. J Neurol Neurosurg Psychiatry 55:8–11

Van der Meché FGA, Oomes PG, Kleyweg RP, Bänffer JRJ, Meulstee J (1991) Axonal Guillain-Barré. Neurology 41:1530

Vedeler CA, Matre R, Nyland H (1988) Class and IgG subclass distribution of antibodies against peripheral nerve myelin in sera

from patients with inflammatory demyelinating polyradiculoneuropathy. Acta Neurol Scand 78:401–407

Walsh FS, Cronin M, Koblar S, Doherty P, Winer J, Leon A, Hughes RAC (1991) Association between glycoconjugate antibodies and Campylobacter infection in patients with Guillain-Barré syndrome. J Neuroimmunol 34:43–51

Weller M, Stevens A, Sommer N, Melms A, Dichgans J, Wiethölter H (1991a) Comparative analysis of cytokine patterns in immunological, infectious, and oncological neurological disorders. J Neurol Sci 104:215–221

Weller M, Stevens A, Sommer N, Wiethölter H, Dichgans J (1991b) CSF interleukins, immunoglobulins, and fibronectin in neuroborreliosis. Arch Neurol 48:837–841

Weller M, Stevens A, Sommer N, Dichgans J, Kappler B, Wiethölter H (1992) Ganglioside antibodies. Lack of diagnostic specificity and clinical utility? J Neurol in press

Wilske B, Schierz G, Preac-Mursic V, von Busch K, Kühlbeck R, Pfister HW, Einhäupl K (1986) Intrathecal production of specific antibodies against Borrelia burgdorferi in patients with lymphocytic meningoradiculitis (Bannwarth's syndrome). J Infect Dis 153:304–314

Yuki N, Yoshino H, Sato S, Miyatake T (1990) Acute axonal polyneuropathy associated with anti-GM1 antibodies following Campylobacter enteritis. Neurology 40:1900–1902