ORIGINAL ARTICLES

Natural history and treatment effects in Guillain-Barré syndrome: a multicentre study

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Abstract

A retrospective multicentre study was performed to investigate the natural history and treatment effects in childhood Guillain-Barré syndrome in a large number of patients. Structured questionnaires were sent to 155 paediatric hospitals for details of patients who conformed to internationally accepted diagnostic criteria and who were treated from spring 1989 to summer 1994. Sixty nine hospitals reported data of 175 patients aged 11 months to 17.7 years. At the height of the disease 26% of the patients remained able to walk, but 16% had to be artificially ventilated. The median time from onset of symptoms to first recovery was 17 days, to walk unaided 37 days, and to be free of symptoms 66 days. There was a large group with a benign and a smaller one with a more protracted course. At long term follow up, 98/106 patients were free of symptoms and the remainder were able to walk unaided. Maximum disability grade was the most powerful prognostic factor. In children unable to walk but not yet tetraplegic, immunoglobulins were able to accelerate recovery. Corticosteroids were less potent. Plasmapheresis

could not be evaluated because it was administered only in the most severe cases. The natural history of Guillain-Barré syndrome in children is extremely variable and more benign than in adults. Treatment with immunoglobulins should be considered in patients unable to walk. Corticosteroids are not as effective and should be withheld except when, in protracted courses, suspicion of chronic inflammatory demyelinating polyneuropathy arises.

(Arch Dis Child 1996; 74: 281-287)

Keywords: Guillain-Barré syndrome, treatment.

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Accepted 14 November 1995

Table 1 Diagnostic criteria of Guillain-Barré syndrome after Asbury and Cornblath¹

- I. Features required for diagnosis
 - (A) Progressive motor weakness of more than one limb
 - (B) Loss of tendon jerks
- II. Features strongly supportive of the diagnosis
 - (A) Clinical features
 1. Progression over four weeks
 2. Relative symmetry of weakness
 3. Mild sensory symptoms or signs
 4. Cranial nerve involvement
 5. Recovery, usually beginning two to four weeks after progression stops
 6. Autonomic dysfunction
 7. Absence of fever at the onset of neuritic symptoms
 - (B) CSF features
 1. CSF protein raised after the first week of symptoms
 2. Counts of 10 or fewer mononuclear leucocytes $\times 10^6/l$
 - (C) Electrodiagnostic features
 - Reduction of conduction velocity, conduction block or abnormal temporal dispersion, increased distal latency or abnormal F wave in more than one nerve
- III. Features casting doubt on the diagnosis
 - (A) Marked, persistent asymmetry of weakness
 - (B) Persistent bladder or bowel dysfunction
 - (C) Bladder or bowel dysfunction at onset
 - (D) More than 50 mononuclear leucocytes $\times 10^6/l$ in CSF
 - (E) Presence of polymorphonuclear leucocytes in CSF
 - (F) Sharp sensory level
- IV. Features that rule out the diagnosis
 - (A) Indication of any metabolic, infectious, or toxic disease associated with polyneuropathy
 - (B) Occurrence of a purely sensory syndrome

CSF=cerebrospinal fluid.

The Guillain-Barré syndrome is an immune mediated acute polyradiculoneuritis most frequently preceded by an unspecific infection. With regard to clinical course and prognosis classical Guillain-Barré syndrome has to be differentiated from variants with accompanying central nervous system inflammation and from chronic inflammatory demyelinating polyneuropathy.¹ More frequently than adults, children recover after a variable span of time. However, during the acute phase of the disease disability can be severe leading to ventilatory insufficiency and even death.

Immunomodulating treatment is performed in a great number of patients, but in children, well controlled studies are lacking. The administration of plasmapheresis and immunoglobulins relies on randomised studies in adults and anecdotal reports or small studies with historical controls in children.²⁻⁸ However, due to the great variability of the natural history, especially in children, studies on a larger scale are clearly needed. Thus, we performed a retrospective multicentre study on the natural history and treatment effects in children with classical Guillain-Barré syndrome.

Patients and methods

We collected reports on children treated for acute Guillain-Barré syndrome from spring 1989 to summer 1994. Questionnaires were sent to 155 paediatric hospitals in Germany and Switzerland for details of patients who conformed to the internationally accepted diagnostic criteria for acute Guillain-Barré syndrome as published by Asbury and

Table 2 Contents of the retrospective Guillain-Barré syndrome questionnaire

Patient
Date of birth, gender, weight
Preceding illness
Clinical diagnosis, serological diagnosis
Progressive phase
Date and kind of first symptoms
Date and findings at admission to hospital
Duration of progression, findings at maximum disability
Paraclinical findings
Date and findings of CSF examination
Date and findings of electrophysiological examination
Treatment
Date, duration, and dosage of corticosteroids, immunoglobulins and plasmapheresis
Date and duration of intubation and artificial ventilation
Recovery phase
Dates of first signs of recovery, time to leave bed, time to walk unaided, time to leave hospital, time to be free of symptoms, last investigation, persisting symptoms, if any

CSF=cerebrospinal fluid.

Cornblath (table 1).¹ Information on the preceeding illness and the course of the disease was collected and is shown in table 2. Signs and symptoms at admission to hospital and at the height of the disease were recorded in a structured way (table 3). The degree of disability was coded in 10 levels (table 4). The levels were defined in a way that could be expected to produce reliable data in a retrospective study.

Descriptive and univariate statistical analysis was performed on a personal computer using the program package SPSS/PC+, version 5. The data were mostly non-normally distributed therefore as a rule non-parametric statistical procedures were used (Mann-Whitney U test, Kruskal-Wallis test, Spearman's rank correlation).

Multivariate analysis was performed on a SUN workstation using SAS procedures LOGISTIC and PHREG. A logistic regression analysis was applied to ordinal target variables (for example maximum disability). This method allows one to interpret the probability of one binary outcome depending on multiple (metric and categorical) influence factors. For k level ordinate variables, one binary variable is generated for each of the k-1 possible cut points. Target variables of the duration type (for example time to recovery) were analysed in a Cox regression model with time dependent covariates. This model postulates that there is one common baseline risk course which is modified by various factors in a time independent manner ('proportional hazard'). The factors of influence, however, may change over time (for example by onset of treatment).

For these statistical calculations, disability at admission and at maximum were coded in 10 levels as indicated in table 4. Progression rate was calculated dividing maximum disability by duration of progression. These variables and

Table 4 Degree of disability

Degree	Definition	At admission (%)	At maximum disability (%)
0	Normal	1.7	0
1	Slight gait disturbance	26.4	8.6
2	Moderate gait disturbance	28.2	17.7
3	Walks holding to furniture	9.2	4.0
4	Walks with help by person	14.4	11.4
5	Not able to walk	9.8	15.4
6	Not able to sit upright	4.0	10.9
7	Tetraparesis	3.4	12.6
8	Tetraplegia	0	3.4
9	Artificial ventilation	2.9	16.0

age were treated as numerical. The other variables were dichotomous (preceeding illness yes/no, treatment yes/no, cerebrospinal fluid protein greater 1000 mg/l yes/no, nerve conduction velocity (NCV) slowing yes/no, NCV compound motor potential reduced yes/no).

Results

Ninety two hospitals responded to the questionnaire. In 23 no patient with Guillain-Barré syndrome had been seen during the preceeding five years. The remaining 69 hospitals reported 184 patients. Nine of them had to be excluded due to a doubtful diagnosis or insufficient data. Thus, 175 children remained for analysis. They all fulfilled the main diagnostic criteria and variable numbers of the additional criteria.

The age of the patients ranged from 11 months to 17.7 years, median 6.3 years. The age distribution was bimodal with peaks at 4 years and 12 years. There was a slight preponderance of boys (n=98) over girls (n=77). In 79% of the patients a preceeding illness was reported. Airway infections (37%) dominated over gastrointestinal infections (11%); in 23% no origin of the febrile illness was determined. In 79% of the patients serological investigations had been performed. In 60% the findings were negative. In the remainder a broad spectrum of infectious agents was found. *Mycoplasma pneumoniae*, cytomegalovirus, Epstein-Barr virus, coxsackievirus, varicella zoster virus, and *Borrelia burgdorferi* were the most frequent with 3% to 6% each. *Campylobacter jejuni* was found in two patients. In four children a vaccination had preceeded the onset of Guillain-Barré syndrome: case 1: diphtheria, tetanus, and pertussis, polio, and *Haemophilus influenzae* B two days earlier; case 2: *H influenzae* B two weeks earlier; case 3: rabies five weeks earlier; and case 4: (früh-sommermeningoencephalitis, early summer meningoencephalitis) 10 days and diphtheria, tetanus, and polio two days earlier.

The first symptoms of Guillain-Barré syndrome were weakness in 43%, ataxia in 27%, and paraesthesias in 28%. Four patients presented with cranial nerve symptoms at the beginning. The children were admitted to hospital at a median of 4 days after the first symptoms (range 0-47 days). The signs and degree of disability at admission are shown in tables 3 and 4; 20% of the patients were already unable to walk and 3% needed artificial ventilation. The disease progressed for a median of 10 days (range 1-35 days) from the

Table 3 Signs and symptoms

	At admission (%)	At maximum disability (%)
Foot drop	56.9	69.5
Ataxia	58.0	68.4
Areflexia	81.0	94.3
Bladder dysfunction	6.9	19.5
Cranial nerve palsy	18.4	35.6
Paraesthesia	32.8	42.0

Table 5 Immunomodulating treatment (the dosage of corticosteroids is given in prednisone equivalents); values are median (range)

	Corticosteroids (n=33)	Immunoglobulins (n=70)	Plasmapheresis (n=19)
Start after first symptom (days)	7 (0-45)	9 (1-50)	12.5 (3-39)
Dosage	2.0 (0.5-5.0) mg/kg BW/day	2.0 (0.2-10.0) g/kg BW total	205 (23-1390) ml/kg BW total
Start before loss of walking	9	19	1
Start before maximum	16	34	5
With corticosteroids	-	12	5
With immunoglobulins	12	-	10
With plasmapheresis	5	10	-

BW=body weight.

beginning. At the height of the disease only 26% of the children were able to walk without support; 16% had to be artificially ventilated. The duration of intubation ranged between 4 and 94 days (median 10 days).

A lumbar puncture was performed in 169 patients 0-60 days (median 6 days) after the start of symptoms. The median protein concentration was 1010 mg/l (10th-90th centile: 300-2640 mg/l), the cell count was 8×10^6 /l (10th-90th centile: $1-54 \times 10^6$ /l). Electrophysiological investigations were performed on day 10 (day 1-230) in 103 patients. NCV findings were reported to be normal in 14%. They showed marked slowing indicative of diffuse demyelination (in the text called 'demyelinated') in 67% and a reduced amplitude of the compound motor potential with normal NCV indicative of mainly axonal dysfunction or distal demyelination (in the text called 'axonal') in 19% of the patients.

Immunomodulating treatment was performed with corticosteroids, intravenous immunoglobulins or plasmapheresis alone or in combination in 96 patients. Dosage and starting time of treatment differed according to local decisions as indicated in table 5.

As a measure of outcome, we calculated the days from the first symptom to the first sign of recovery, to first being able to leave bed, to walk without support, to leave the hospital, and to be free of all symptoms (table 6).

Sixty three per cent of the patients could be followed up after discharge from hospital. When examined at least six months later, the clinical findings in 98 of 106 children were completely normal. Three still exhibited slight and three moderate weakness of the lower extremities and two still complained of incoordination of gait. All were able to walk unaided. Comparing these 106 children with the 69 without follow up information, the maximum disease severity in the acute phase had not been different. Thus, the group with long term follow up can be considered representative for the whole sample of patients.

With the aim to delineate prognostic criteria

and the effects of treatment, we first performed univariate statistical analyses. Single clinical findings at admission to hospital had no predictive value for the maximal disease severity. However, a higher degree of disability at admission correlated to a higher maximal disability (Spearman's correlation 0.39, $p < 0.001$).

At the height of the disease, there was a significant correlation of bladder dysfunction ($p < 0.001$), cranial nerve palsies ($p < 0.001$), and a sensory deficit ($p < 0.01$) with the degree of disability and the necessity of artificial ventilation.

'Axonal' NCV changes, compared with signs of diffuse demyelination or normal values, were found in older patients (median 13 v 6 years, $p < 0.02$). They were indicative of a longer duration until freedom from symptoms (median 106 v 62 days, $p = 0.06$).

There was a correlation of the maximum disability and a smaller one of the disability at admission with the outcome measures, with the exception of the time of the first signs of recovery (table 7, fig 1). A higher rate of progression (maximum disability divided by the duration of progression) was correlated to a shorter time to the first sign of recovery (Spearman's correlation -0.35, $p < 0.001$), but to a longer time to discharge (Spearman's correlation 0.46, $p < 0.001$) and to be free of symptoms (Spearman's correlation 0.31, $p < 0.01$).

Comparing the parameters of disease severity between the treatment groups (table 8), an apparent influence of the age of the children and disease severity on the decision to treat was seen. Plasmapheresis was performed in older individuals with a very high disability (75% on ventilator). Progression rate correlated with the decision to perform plasmapheresis ($p < 0.001$). The group without any treatment consisted of young children with low severity (only 2.5% on ventilator). Thus, comparing treatment effects, controlling disease severity is absolutely necessary.

Regarding the effect of disease severity and the treatment modalities on the outcome variables, a positive effect of intravenous immunoglobulins on the time to leave bed (median 18 v 23 days, $p < 0.01$) and to walk unaided (median 23.5 v 33 days, $p = 0.05$, fig 2) was demonstrated in children unable to walk, but not in those with tetraplegia or requiring artificial ventilation. No benefit of corticosteroids was demonstrated. The same is true for plasmapheresis, which was only applied in the most severe cases.

As treatment specific outcome measures, we additionally evaluated the time from the initiation of treatment to the first signs of recovery and to regaining independent walking. Between the groups treated with intravenous immunoglobulins or corticosteroids only, duration and rate of progression, maximum disability, the time of the initiation of treatment, and the time of first recovery were not different. However, walking ability returned significantly earlier after immunoglobulins than after corticosteroids ($n = 33/13$, median 14 v 38 days, $p < 0.03$). The effect of

Table 6 Time course of recovery

Days from first symptom to	No	Median	Minimum	Centiles		Maximum
				10th	90th	
First sign of recovery	168	17	1	7	34	61
Leave bed	85	23	3	14	63	107
Walk unaided	108	37	4	16	85	199
Leave hospital	174	28	2	10	68	256
Be free of symptoms	105	66	2	22	181	790

Table 7 Disease severity and outcome measures (Spearman's correlation coefficient)

	First sign of recovery	Leave bed	Walk unaided	Leave hospital	Be free of symptoms
Disability at admission	-0.07	0.00	0.12	0.16	0.21
Disability at maximum disability	-0.03	0.41 $p<0.001$	0.46 $p<0.001$	$p<0.03$ 0.58 $p<0.001$	$p<0.03$ 0.46 $p<0.001$

plasmapheresis could not be compared due to the higher disease severity.

The interpretation of the univariate analyses is complicated by the retrospective study design with variable treatment indications and multiple medications in part of the patients. Thus we performed an additional multivariate analysis to control for multiple covariates.

In a backward elimination procedure, logistic regression analysis revealed that from seven entered variables (age, preceeding illness, rate of progression, disability at admission, NCV finding demyelinated and axonal, cerebrospinal fluid protein raised) three had influenced the physician's decision to treat. A higher age of the patient ($p<0.02$, odds ratio 1.10 for an increase of one year) and a higher disability at admission ($p<0.03$, odds ratio 1.23 for an increase of one level) were reasons to treat with any measure. The decision to perform plasmapheresis depended on age ($p<0.01$, odds ratio 1.28 for an increase of one year) and the rate of progression ($p<0.001$, odds ratio 6.25 for an increase of one unit).

Looking for predictive variables of maximum disability, ordinal logistic regression analysis showed that it mainly depended on a high disability already present at admission ($p<0.001$, odds ratio 1.70 for an increase of one level). The treatment with corticosteroids ($p<0.02$, odds ratio 4.00), intravenous immunoglobulins ($p<0.01$, odds ratio 3.12), and plasmapheresis ($p<0.001$, odds ratio 125.0) indicated a higher maximum disability, apparently due to the correct estimation of the clinical course and treatment decision by the attending physicians. Preceding illness, rate of progression before admission, age, and the cerebrospinal fluid and NCV findings were not predictive.

Investigating the effect of disease and treatment variables on the outcome measures by Cox regression (table 9), a strong negative

Figure 1 Life table analysis of the time to become free of symptoms by maximum disability ($p<0.001$); children always able to walk, median 62.2 days; not able to walk, median 86.7 days; and tetraplegic/ventilated, median 113.5 days.

effect of the maximum disability was confirmed. Controlling the maximum disability, a high rate of progression was indicative of a shorter time to first recovery, to leave the hospital, and to be free of symptoms. A cerebrospinal fluid protein concentration greater than 1000 mg/l and signs of axonal damage or distal demyelination in NCV testing had a negative influence on some of the outcome measures. Treatment with intravenous immunoglobulins and corticosteroids was shown to accelerate recovery in the early phase, but not later in enabling patients to leave hospital and to become free of the last symptoms.

Discussion

Performing this retrospective multicentre study we had to choose definitions of disability and outcome variables that could be expected to be deducible from the hospital charts with a reasonable degree of reliability. However, we had to accept that not all variables would have the same high reliability.

Despite this, our epidemiological and natural history data are nearly identical with previously published findings of epidemiological studies and single centre studies on childhood Guillain-Barré syndrome. Children are different from adults in that the incidence seems to be higher with a younger age.⁹⁻¹¹ In even more children than adults an acute infection preceded the neurological symptoms. In adults a high frequency of *C jejuni* and cytomegalovirus infections has been found,^{12,13} but no systematic serological investigations in children have been published so far.

Besides weakness and ataxia, limb and back pain are frequent initial symptoms of Guillain-Barré syndrome, especially in older children. After a progressive phase of up to 35 days' duration, 30% to 40% of children remain able to walk with or without assistance compared with only 19% of adults.¹⁴ Altogether 15% to 20% of the children need artificial ventilation and 35% to 45% show an impairment of cranial nerve function.^{9,11,15-20} These latter figures are comparable with the findings in adults.^{12,21}

With our retrospectively collected electrophysiological data from a large number of investigators we are not able to contribute to the discussion whether a purely axonal Guillain-Barré syndrome in children really exists. A reduction of the compound motor potential amplitude with normal NCV can be due to an axonal damage or to distal demyelination. Children showing this feature were older and recovered more slowly than the other ones. However, in our study, as in the experience of others,¹⁹ a reduced compound motor potential is not an indicator of a bad functional outcome in the long term.

Data on the course of recovery in our patients are better than in the literature. Briscoe *et al* reported a mean time of recovery after reaching the maximum disability of the disease of 19.3 days (5-46 days).¹⁶ In our study the first sign of recovery was seen after a median of 17 days

Table 8 Evolution and severity of disease in the treatment groups; values are median

	No treatment (n=79)	Corticosteroids (n=33)	Immunoglobulins (n=70)	Plasmapheresis (n=19)
Age	5.1	7.4	7.0	10.9
Days before admission	5.0	5.0	4.0	2.0
Disability at admission (degrees) ^a	2.0	2.5	2.5	3.5
Duration of progression (days)	8.5	12.0	10.0	7.0
Disability at maximum disability (degrees)	4.0	7.0	6.0	9.0
Rate of progression (degree/day)	0.6	1.0	1.2	4.5

^aDegree of disability defined in table 4.

Figure 2 Time to regain the capacity of unaided walking as a function of maximum disability (degree 3–6 v 7–9) and treatment group (treatment without v treatment with intravenous immunoglobulins). IVIg=intravenous immunoglobulins.

from onset of the disease. The mean time to be free of symptoms reported in the literature is 120 to 180 days.^{11 16 18 19} Our patients were free of symptoms at a median of 64 days. In our experience, there is a large number of patients with a favourable prognosis and a smaller one with a more protracted course. Thus, reporting the outcome in Guillain-Barré syndrome as mean and standard deviation is inadequate because of the non-normal distribution of the data. The mean values could overestimate the more appropriate median by nearly 50%. Furthermore, in most published studies the experiences of referral centres and teaching hospitals are reported. Thus, a selection of more severe cases has to be considered whereas our study includes a large number of patients with a less severe course treated in local hospitals.

After a variable time of follow up, all children with acute Guillain-Barré syndrome reported in the literature were able to walk unaided. Altogether 20% to 25% still exhibited some degree of weakness and loss of reflexes not interfering with daily life and participating

Table 9 Cox proportional hazard regression with time dependent covariates; risk ratios only for significant covariates ($p<0.05$) are given*

Covariate	No of levels	First sign of recovery	Leave bed	Walk unaided	Leave hospital	Be free of symptoms
Age	Years	0.96	—	—	0.96	—
CSF protein >1000 mg/l	2	—	—	0.58	0.71	—
NCV 'axonal'	2	—	—	—	—	0.37
Rate of progression	Units	1.91	—	—	1.50	1.65
Maximum disability	10	0.85	0.66	0.57	0.76	0.71
Corticosteroids	2	2.65	5.60	1.75	—	—
Immunoglobulins	2	2.40	2.97	2.10	—	—

*The risk ratio is the relative chance to improve in the next time period for each level of the independent covariate – that is, by an increase of one level of maximum disability the chance to start improving in the next time period is reduced by the factor of 0.85 and by treatment with immunoglobulins it is increased by the factor of 2.4. CSF=cerebrospinal fluid.

in sports.^{11 18 19 22} Chronic or relapsing courses were rarely reported and then usually after a subacute and protracted onset.¹⁶ We observed such a course in only two of our patients who were excluded from further analysis. Thus, the prognosis of Guillain-Barré syndrome in children is significantly better than in adults. Winer *et al*, after one year, found only 67% of adults to be free of symptoms and 20% to be still significantly disabled¹⁴; 10% had died due to consequences of the polyneuropathy. The main prognostic factors for a bad outcome had been an age of more than 40 years, a short time to become bedridden, reduced compound motor potential, and the necessity of ventilation. In children, the need for artificial ventilation does not exclude a complete recovery.^{16 17}

In our study, the velocity of recovery and the persistence of symptoms at follow up were related to the maximum disease severity. Using multivariate statistical methods we were able to show that treatment with corticosteroids and intravenous immunoglobulins had also contributed to a shorter time to first recovery, to leave bed, and to walk unaided.

Treatment with corticosteroids in classical Guillain-Barré syndrome has not been studied in children so far. They are frequently of value in children with a subacute onset of symptoms and a protracted course.^{23–25} In adults, after conflicting older studies, a randomised study with high dose intravenous methylprednisone in acute Guillain-Barré syndrome showed no effectiveness.²⁶ As result of a pilot study, van de Meche *et al* of the Dutch Guillain-Barré Study Group reported superior results with intravenous immunoglobulins plus corticosteroids than with immunoglobulins alone.²⁷ In our univariate analysis, the effect of corticosteroids was inferior to immunoglobulins. We found no indication that the combination with intravenous immunoglobulins increased the effectiveness.

As a result of two large randomised studies, plasmapheresis is the treatment of choice in adults with severe Guillain-Barré syndrome. The chance to improve at least one disability grade after four weeks, the duration of artificial ventilation, the time to regain the ability to walk independently, and the chance to regain full strength after one year are influenced significantly.^{2 3} In children, no randomised studies have been performed. Epstein and Sladky compared nine children unable to walk independently who were treated with plasmapheresis with 14 historical controls.²⁸ The mean maximal disability was comparable. The mean (SD) time to regain independent walking after treatment was 24.0 (25.4) days and in the control group it was 60.2 (43.6) days. Further studies on some 60 children treated with plasmapheresis reported a very variable mean time to walk unaided of between 16 and 70 days,²⁹ and Hammersjö questioned the value of performing plasmapheresis in childhood Guillain-Barré syndrome.³⁰

Starting in 1988,³¹ a still increasing number of reports on a beneficial effect of intravenous immunoglobulins has been published. In adults unable to walk independently, treatment with

immunoglobulins resulted in amelioration of symptoms in 18/25, 6/7, and 7/14 cases within three to 21 days.³²⁻³⁴ However, other authors stressed a high rate of treatment failures and relapses.^{35,36}

In 1992 a randomised study comparing plasmapheresis and intravenous immunoglobulins in adults unable to walk unaided for 10 metres was published. The results indicated a slight benefit of immunoglobulins over plasmapheresis.⁵ It is important to note that in both treatment groups 10% of patients experienced fluctuation of symptoms some 14 days after treatment that frequently responded to a second treatment course. Twenty five per cent of the immunoglobulin group and 34% of the plasmapheresis group were non-responders.^{37,38} This study has been criticised for methodological reasons and because the results of the plasmapheresis group were significantly worse than in the French and American trials.^{39,40} Further studies in adults are underway.⁴¹

In children, single cases with rapid improvement during administration of intravenous immunoglobulins or within four days have been observed.^{4,6,42-45} In reports including a larger number of children, the mean time to independent walking was two to 42 days, most frequently between 15 and 20 days.^{7,29,46} This was considered better than the findings in historical controls with no treatment,⁷ with corticosteroids,⁴⁷ and even with plasmapheresis.²⁹ The best results have been reported by Shahar *et al.*⁴⁸ Twenty three children unable to walk were treated with 2 g immunoglobulin/kg body weight in two days. Twenty two improved two disability grades within two weeks and 18 regained the ability to walk within one week after treatment.

Gürses *et al* reported the interval from onset of the disease to maximum symptoms and from maximum symptoms to improvement to be significantly shorter in children treated with 2 g of immunoglobulin than in untreated ones.⁴⁹ The patients had been included in the groups according to the sequence of admission. However, the time differences were rather short (three and four days as a mean) and no clear description of the degree of disability at the start of treatment was given.

Our study has confirmed the treatment effect of intravenous immunoglobulin. However, given the retrospective study design, it is not possible to delineate a clear indication when and which patient to treat. We have the impression that the benefit of intravenous immunoglobulins is greatest in children who are unable to walk independently but not yet tetraplegic and ventilated. No answer to the question as to whether treatment starting earlier is of value is yet possible.

In young children with severe Guillain-Barré syndrome, due to easier performance and fewer side effects,⁵ paediatricians probably will prefer treatment with intravenous immunoglobulins to plasmapheresis. However, the possible consequences of high dose immunoglobulins have to be kept in mind. These have been reported as severe immunological

reaction in IgA deficiency, increased intracranial pressure and aseptic meningitis, thromboembolic stroke, and renal failure.⁵⁰⁻⁵³ Although in our study corticosteroids were also shown to be of value, their effectiveness seems to be inferior to immunoglobulins. This and the consequences of immunosuppression in severely disabled children should preclude their use as a drug of first choice.

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Addendum

We are indebted to all colleagues who have contributed patients to our study – Kotlarek: Aachen; Elsbroek, Friedrich: Ahlen; Joppich: Amberg; Elschner, Heidemann: Augsburg; Menner: Bad Herfeld; Wenzel, Deeg: Bamberg; Hellmann, Hübner: Berlin; Penzien, Vassella: CH-Bern; Schara, Görke: Bochum; Schmidt, Teufel: Boblingen; Hofmann: Chemnitz; Lang: Coesfeld; Dittmer, Oppermann: Cottbus; Wemmer: Darmstadt; Vallo, Wesseler: Detmold; Strehl, Diekmann: Dortmund; Todt: Dresden; Baethmann, Voit, Lenard, Scheele, von Lilien-Waldau: Düsseldorf; Sauter, Helwig, Korinthenberg, Freiburg; Evers: Gelsenkirchen; Neuhäuser: Gießen; John, Reinken: Hamm; Greve, Natzschka: Hannover; Benninger, Rating: Heidelberg; von Brenndorf: Heidenheim; Degener, Cremer: Heilbronn; Jost, Sitzmann: Homburg; Schächtele, Schindera: Karlsruhe; Geiger, Wehinger: Kassel; Nafziger-Straub, Kehr: Kempten; Stephani: Kiel; Rister: Koblenz; Kratzer: Konstanz; Hörschemeyer, Schulte-Wissermann: Krefeld; Pröbsting: Landshut; Borte: Leipzig; Schmiedlau, Uhle: Lippstadt; Dominick: Ludwigshafen; Wässer, Kruse: Lubeck; Schmitt-Mechelke: CH-Luzern; Ebinger, Reitter: Mainz; Koelfen, Niessen: Mannheim; Trinczek-Gärtner, Schöber, Häßler, Emmrich, Snigula, Tympner: München; Feil, Hoovey, Uekötter: Münster; Henrichs: Neuburg; Wagner, Gellissen: Neuwied; Gerken: Oldenburg; Rickers: Osnabrück; Rantala: SF-Oulu; Kauther: Paderborn; Berbig: Saalfeld; Heye: Siegen; Oßwald: Singen; Brand, von Schnakenburg: St Augustin; Keimer, Köhler: Stuttgart; Scheel, Michaelis: Tübingen; Pussert, Teller: Ulm; Karstens, Franke: Vechta; Huenges: Villingen-Schwenningen-Albani; Wiesbaden; Koepf: Wismar; Straßburg: Würzburg; Mortier: Wuppertal.