Long-term Clinical Outcome After Lyme Neuroborreliosis in Childhood

WHAT’S KNOWN ON THIS SUBJECT: Persistent facial nerve palsy is a well-described neurologic deficit after Lyme neuroborreliosis and occurs in 13% to 20% of children. Other neurologic deficits are less closely described. Nonspecific subjective symptoms are reported as often among patients as controls in previous short-term follow-up studies.

WHAT THIS STUDY ADDS: Persistent neurologic deficits, other than facial nerve palsy, were found in 14% of patients, causing impaired fine motor skills, poor balance, or persistent pain. Nonspecific subjective symptoms were reported as often among patients as controls in this long-term follow-up study and should not be considered as sequelae after Lyme neuroborreliosis.

OBJECTIVES: To determine long-term clinical outcome in children with confirmed Lyme neuroborreliosis (LNB) and to evaluate persistent subjective symptoms compared with a control group.

METHODS: After a median of 5 years, 84 children with confirmed LNB underwent a neurologic re-examination, including a questionnaire. Medical records were analyzed, and a control group (n = 84) was included.

RESULTS: The total recovery rate was 73% (n = 61). Objective neurologic findings, defined as “definite sequelae,” were found in 16 patients (19%). The majority of these children had persistent facial nerve palsy (n = 11), but other motor or sensory deficits occurred (n = 5). Neurologic signs and/or symptoms defined as “possible sequelae” were found in another 7 patients (8%), mainly of sensory character. Nonspecific subjective symptoms were reported by 35 patients (42%) and 32 controls (38%) (nonsignificant). Affected daily activities or school performance were reported to the same extent in both groups (23% vs 20%, nonsignificant).

CONCLUSIONS: The long-term clinical recovery rate was 73% in children with confirmed LNB. Persistent facial nerve palsy occurred in 13%, whereas other motor or sensory deficits were found in another 14%. Neurologic deficits did not affect daily activities or school performance more often among patients than controls and should be considered as mild. Furthermore, nonspecific subjective symptoms such as headache, fatigue, or memory or concentration problems were reported as often among patients as controls and should not be considered as sequelae after LNB. Pediatrics 2012; 130:262–269

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KEY WORDS: Lyme borreliosis, neuroborreliosis, children, clinical outcome, sequelae, facial nerve palsy, persistent symptoms

ABBREVIATIONS: CSF—cerebrospinal fluid, EM—erythema migrans, Ig—immunoglobulin, LB—Lyme borreliosis, LNB—Lyme neuroborreliosis

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Lyme borreliosis (LB) is the most common tick-borne infection in Europe and the United States, and it is caused by the spirochete *Borrelia burgdorferi*. The infection may give rise to a variety of symptoms by affecting different organs such as the skin, joints, heart muscle, or nervous system. The typical red skin lesion erythema migrans (EM) is the most frequent manifestation of LB in both children and adults. In Lyme neuroborreliosis (LNB), when the nervous system is affected, acute peripheral facial nerve palsy and subacute meningitis are the most common neurologic manifestations, but other cranial or peripheral neuropathies may occur. Neurologic signs and symptoms may not be specific, and the diagnosis LNB requires laboratory confirmation with mononuclear pleocytosis in the cerebrospinal fluid (CSF) and intrathecally produced *Borrelia*–specific antibodies, according to European guidelines.

The duration of symptoms at diagnosis is of importance for the occurrence of *Borrelia*–specific antibodies in the CSF, and in pediatric patients with short duration of symptoms, as in early LNB, the diagnosis may, according to these guidelines, not always be confirmed. Therefore, children with facial nerve palsy, mononuclear pleocytosis in CSF, and *Borrelia*–specific antibodies in serum (or a recent or present EM) are strongly suspected to have LNB and should be treated as such. LNB is effectively treated with antibiotics. The prognosis in children is considered better than in adults, but some neurologic symptoms may persist. In children, persistent facial nerve palsy was found in 13% to 20% post LNB treatment causing eye-closing problems, pronunciation difficulties, and cosmetic complaints. However, prognostic factors of importance for total recovery of facial nerve palsy have not been identified in children.

Persistent symptoms post LNB treatment occur more frequently in adult patients than in controls, but repeated antibiotic treatment has not been found to improve persistent symptoms or neurocognitive problems. Persistent symptoms post LNB treatment are generally less frequent in children than in adults. In a recent study, nonspecific symptoms in children 6 months post LNB treatment were not reported more frequently among patients than controls. Large long-term follow-up studies of strictly classified and representative pediatric LNB cases, including a structured neurologic re-examination, an otoneurologic re-evaluation, a questionnaire for self-reported symptoms, and an age-matched control group, have not to our knowledge been carried out in children previously.

The aim of this study was to determine long-term clinical outcome in children with confirmed LNB and to evaluate persistent subjective symptoms as compared with a control group.

**METHODS**

**Subjects**

Patients diagnosed as confirmed cases of LNB at 3 major pediatric clinics in southeast Sweden during the period 1996–2002 were invited to participate in this long-term follow-up study. A total of 146 LNB cases were identified when diagnosis was based on strict case definition of LNB (see below). Children and parents (or guardians) were invited to attend a follow-up re-examination and to complete a questionnaire. Eighty-six patients (n = 86) agreed to participate (response rate 59%). Clinical data from medical records were analyzed by using the patients’ unique personal identification numbers.

Thirty-three patients did not want to participate (n = 33), and an additional 27 patients did not answer the request despite being contacted twice by mail and once by telephone. Two patients were excluded because of comorbidity that would complicate the re-evaluation, such as congenital myelomeningocele (n = 1) and mental retardation (n = 1). Participants (n = 84) did not differ regarding age and gender as compared with nonparticipants (n = 62).

A control group of children, representing a random sample of the Swedish population, was obtained from the Swedish National Register of Statistics. They were matched for age, gender, and area of living (n = 84). They reported no known tick bites, no symptoms, or previous treatment of LB. Controls were not examined by a physician or tested for *Borrelia* serology.

**Patient Characteristics and Clinical Manifestations on Admission**

Median age was 7 years (2–14 years) on admission. Gender distribution was equal, and the median duration of symptoms before start of treatment was 10 days (1–365 days) (Table 1). Most patients experienced 2 or more symptoms at presentation (median, 4 symptoms; range, 1–10 symptoms). The major clinical manifestations and CSF findings are shown in Table 1.

All patients were treated with antibiotics for 10 to 14 days (Table 1), and all patient samples for laboratory diagnosis were drawn before the start of antibiotic treatment.

No patient reported a history of major neurologic symptoms or known neurologic diagnosis before the present LNB evaluation.

**Case Definition and Inclusion Criteria**

The diagnosis of confirmed LNB was defined according to the European clinical case definition: that is, neurologic symptoms attributable to LNB, pleocytosis in CSF (>5 × 10^6 mononuclear cells/L), and intrathecally produced immunoglobulin M (IgM) and/or
TABLE 1 Characteristics and Clinical Data From Patients With Confirmed LNB on Admission (n = 84)

<table>
<thead>
<tr>
<th>Characteristics and Clinical Data</th>
<th>Values</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, y, median (range)</td>
<td>7 (2–14)</td>
</tr>
<tr>
<td>Gender, n (%)</td>
<td></td>
</tr>
<tr>
<td>Boy</td>
<td>44 (52)</td>
</tr>
<tr>
<td>Girl</td>
<td>40 (48)</td>
</tr>
<tr>
<td>Major clinical manifestations, n (%)</td>
<td></td>
</tr>
<tr>
<td>Facial nerve palsy</td>
<td>53 (63)</td>
</tr>
<tr>
<td>Headache</td>
<td>46 (55)</td>
</tr>
<tr>
<td>Fatigue</td>
<td>37 (44)</td>
</tr>
<tr>
<td>Neck pain or stiffness</td>
<td>24 (29)</td>
</tr>
<tr>
<td>Loss of appetite or nausea</td>
<td>26 (21)</td>
</tr>
<tr>
<td>Fever</td>
<td>18 (19)</td>
</tr>
<tr>
<td>EM</td>
<td>11 (13)</td>
</tr>
<tr>
<td>Vertigo</td>
<td>10 (12)</td>
</tr>
<tr>
<td>Pain, numbness, or weakness in extremity</td>
<td>7 (8)</td>
</tr>
<tr>
<td>No. of symptoms per patient, median (range)</td>
<td>4 (1–10)</td>
</tr>
<tr>
<td>Duration of symptoms, days, median (range)</td>
<td>10 (1–365)</td>
</tr>
<tr>
<td>CSF findings</td>
<td></td>
</tr>
<tr>
<td>Mononuclear pleocytosis, median (range)a</td>
<td>378 (6–713)</td>
</tr>
<tr>
<td>Anti-Borrelia antibodies, n (%)a</td>
<td>24 (29)</td>
</tr>
<tr>
<td>IgM, n (%)a</td>
<td>17 (20)</td>
</tr>
<tr>
<td>Anti-Borrelia antibodies, n (%)a</td>
<td>43 (51)</td>
</tr>
<tr>
<td>Antibiotic treatment, n (%)</td>
<td></td>
</tr>
<tr>
<td>Ceftriaxone, IV</td>
<td>43 (52)</td>
</tr>
<tr>
<td>Penicillin, IV</td>
<td>7 (8)</td>
</tr>
<tr>
<td>Doxycycline, po</td>
<td>34 (40)</td>
</tr>
<tr>
<td>Confirmed LNB diagnosis, n (%)b</td>
<td>84 (100)</td>
</tr>
</tbody>
</table>

LNB, lyme neuroborreliosis; EM, erythema migrans; CSF, cerebrospinal fluid; IV, intravenous; po, per oral.

TABLE 2 Definition of Neurologic Sequelae After LNB

<table>
<thead>
<tr>
<th>Definitions</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Definite sequelae</td>
<td>Objective neurologic findings that correlate well in character and time with the LNB diagnosis</td>
</tr>
<tr>
<td>Possible sequelae</td>
<td>Neurologic signs and/or symptoms that are nonspecific but correlate in character and time with the LNB diagnosis</td>
</tr>
<tr>
<td>No sequelae</td>
<td>No neurologic signs or symptoms, or subjective symptoms that are nonspecific and do not correlate in character or time with the LNB diagnosis</td>
</tr>
</tbody>
</table>

LNB, lyme neuroborreliosis.

An enzyme-linked immunosorbent assay based on the B burgdorferi flagella antigen was used for antibody index detection in CSF (DAKO Neuroborreliosis kit K6028, Glostrup, Denmark) to ensure intrathecal produced Borrelia-specific antibodies.26

**Re-examination**

At the follow-up visit, a thorough neurologic re-examination, according to a standardized protocol, was carried out by a pediatrician (Drs Skogman, Nordwall, or Ekelund; see Acknowledgment) according to European guidelines.9 Oto-neurologic examination was carried out by an ear-nose-throat specialist (Drs Ödkvist or Wick, see Acknowledgment) according to the House-Brackmann grading system,27 oto-microscopy, investigation with Frenzel glasses (for head shake nystagmus), and a caloric test. Both protocols were discussed beforehand to ensure equal interpretations of otological and neurologic findings.

**Questionnaire**

All patients and/or their parents (or guardians) completed a questionnaire at the follow-up visit with questions concerning current symptoms of facial nerve palsy, headache, fatigue, neck pain or stiffness, vertigo, symptoms from extremities, loss of appetite or weight loss, memory or concentration problems, or sleeping disorders, and whether these symptoms affected daily activities or performance at school. Furthermore, the questionnaire included information about known tick bites, physician diagnosed re-infection of LB, and antibiotic treatment of LB during the follow-up period. A similar questionnaire was completed by children and/or parents (or guardians) in the control group and returned by mail.

**Definition of Sequelae**

The definition of neurologic sequelae after LNB needed to be strictly defined to correctly evaluate neurologic signs and symptoms among patients at follow-up. Definitions of “definite sequelae,” “possible sequelae,” or “no sequelae” are presented in Table 2.

**Statistical Analysis**

SPSS software (SPSS Inc, Chicago, IL), version 15.0, was used for statistical calculations. The Mann–Whitney U test and χ² or Fisher’s exact test were used when comparing groups. Level of significance was P < .05.

**Ethics**

The study was approved by the Regional Committee of Medical Research Ethics at the Faculty of Health Sciences, Linköping University (Dnr 03-548 and M184-06). Informed written consent was obtained from children and parents (or guardians).

**RESULTS**

**Patient Characteristics at Follow-up**

The median age at follow-up was 13 years, and the median time between LNB diagnosis and follow-up was 5 years (Table 3). Data on known tick bites, re-infection, and antibiotic treatment of LB during follow-up are shown in Table 3. No patient reported progressive neurologic symptoms, and no patient had been diagnosed with other neurologic diagnosis during the follow-up period.

**Otoneurologic Re-evaluation**

Eleven of 53 patients with acute facial nerve palsy at diagnosis had persistent facial nerve palsy at follow-up (21%) (no. 1–11, Table 4). The facial nerve dysfunction was moderate in the 11 cases that
TABLE 3  Clinical Outcome in Patients With Confirmed LNB at Follow-up (n = 84)

<table>
<thead>
<tr>
<th>Variables</th>
<th>Values</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, y, median (range)</td>
<td>12 (7–19)</td>
</tr>
<tr>
<td>Time to follow-up, y, median (range)</td>
<td>5 (3–8)</td>
</tr>
<tr>
<td>Known tick bite, n (%)</td>
<td>53 (63)</td>
</tr>
<tr>
<td>Re-infection of LB, n (%)</td>
<td>1 (1)</td>
</tr>
<tr>
<td>Facial nerve palsy</td>
<td>1 (1)</td>
</tr>
<tr>
<td>Antibiotic re-treatment of LB, n (%)</td>
<td>2 (2)</td>
</tr>
<tr>
<td>Clinical outcome, n (%)</td>
<td>16 (19)</td>
</tr>
<tr>
<td>Definite sequelae</td>
<td>7 (8)</td>
</tr>
<tr>
<td>No sequelae</td>
<td>61 (73)</td>
</tr>
<tr>
<td>Affected daily activities or school performance, n (%)</td>
<td>6 (37)</td>
</tr>
<tr>
<td>Definite sequelae</td>
<td>4 (57)</td>
</tr>
<tr>
<td>No sequelae</td>
<td>9 (15)</td>
</tr>
</tbody>
</table>

LNB, lyme neuroborreliosis; LB, lyme borreliosis; EM, erythema migrans.

a One or more tick bites during the follow-up period.

b Physician diagnosed re-infection during the follow-up period.

c Defined as in Table 2.

is, grades 3 to 4 according to the Hourse-Brackmann grading system (Table 4). One or several branches of the facial nerve were affected (forehead, orbital, or oral area), but no child had a severe or total loss of facial nerve function. One child had bilateral facial nerve palsy (no. 1). Four children had synkinesias (no. 1, 4, 6, and 7), which are involuntary simultaneous movements in the orbital and oral areas that originate from defect sprouting in the nerve regeneration process. Eye closing impairment, excessive tear secretion, pronunciation difficulties, cosmetic complaints, and social problems were reported as consequences of the facial nerve dysfunction. Some children showed signs of balance nerve dysfunction, such as deviant caloric test (no. 12), head shake nystagmus (no. 17 and 19), and prominent end position nystagmus (no. 21) (Table 4).

Neurologic Re-examination

Objective neurologic findings, defined as definite sequelae, were found in 16 patients (19%) at follow-up (Table 4). Some children (n = 11) had persistent facial nerve palsy (no. 1–11), but other neurologic deficits were also found, such as persistent neuropathy (no. 12), trigeminal neuropathy (no. 13), hemiparesis after an LNB associated stroke (no. 14), polyneuropathy (no. 15), and peroneal nerve palsy (no. 16) (Table 4). Pathologic Romberg’s test (ie, postural unsteadiness as a sign of poor balance) was found in 3 patients (no. 3, 10, and 16), of whom 2 also reported vertigo as a subjective symptom. Impaired finger opposition affecting fine motor skills such as writing was found in 3 patients (no. 4, 12, and 15). Sensory deficit was found in 1 patient with impaired facial sensitivity to touch (no. 13) and 1 patient with impaired sense of vibration (no. 15).

Seven patients (n = 7) were classified as possible sequelae (8%) with persistent nonspecific neurologic signs and/or symptoms that correlated in character and time after the LNB. Findings were mainly of sensory character in 7 patients (Table 4). The sequelae were found in 7 patients (19%) and possible sequelae were found in 7 patients (8%) (Tables 3 and 4). The sequelae were of motor character in 8 patients, sensory character in 8 patients, and both motor and sensory character in 7 patients (Table 4). Age, gender, durations of symptoms on admission, or antibiotic treatment did not differ significantly between patients with no sequelae as compared with patients with definite sequelae or possible sequelae (data not shown).

Clinical Outcome

The total recovery rate was 73% in patients with LNB at follow-up (Table 3). Definite sequelae were found in 16 patients (19%) and possible sequelae were found in 7 patients (8%) (Tables 3 and 4). The sequelae were of motor character in 8 patients, sensory character in 8 patients, and both motor and sensory character in 7 patients (Table 4). Age, gender, durations of symptoms on admission, or antibiotic treatment did not differ significantly between patients with no sequelae as compared with patients with definite sequelae or possible sequelae (data not shown).

DISCUSSION

In this long-term follow-up study of children with confirmed LNB, the total recovery rate was 73%. The major objective neurologic finding was, as expected, persistent facial nerve palsy. One-fifth (21%) of patients with acute facial nerve palsy at LNB diagnosis had persistent, but partial, facial nerve...
## TABLE 4 Patients With Neurologic Sequelae After LNB (n = 23)

<table>
<thead>
<tr>
<th>Patient No.</th>
<th>Age, y</th>
<th>Neurologic Examination</th>
<th>Subjective Symptoms</th>
<th>Definition of Sequelae</th>
<th>Character of Sequelae</th>
<th>Consequence of Sequelae</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>18</td>
<td>FNP, bilateral; left (3, 3, 3); right (3, 3, 3); synkinesia</td>
<td>0</td>
<td>Smile asymmetry</td>
<td>Definite Motor</td>
<td>Persistent FNP; cosmetic problems</td>
</tr>
<tr>
<td>2</td>
<td>13</td>
<td>FNP, left (1, 1, 3)</td>
<td>0</td>
<td>Eye closing impairment; dry eyes</td>
<td>Definite Motor</td>
<td>Persistent FNP; eye problems</td>
</tr>
<tr>
<td>3</td>
<td>15</td>
<td>FNP, left (1, 1, 3); synkinesia</td>
<td>Pathologic; Romberg's test</td>
<td>Vertigo; nausea</td>
<td>Definite Motor + sensory</td>
<td>Persistent FNP; poor balance</td>
</tr>
<tr>
<td>4</td>
<td>13</td>
<td>FNP, right (3, 3, 3); synkinesia</td>
<td>Dysdiadocho-kinesia</td>
<td>Smile asymmetry</td>
<td>Definite Motor</td>
<td>Persistent FNP; social problems; impaired fine motor skills</td>
</tr>
<tr>
<td>5</td>
<td>14</td>
<td>FNP, left (1, 1, 3)</td>
<td>0</td>
<td>Eye-closing impairment</td>
<td>Definite Motor</td>
<td>Persistent FNP; eye problems</td>
</tr>
<tr>
<td>6</td>
<td>13</td>
<td>FNP, left (3, 1, 3); synkinesia</td>
<td>Pathologic; Romberg's test</td>
<td>Headache</td>
<td>Definite Motor</td>
<td>Persistent FNP; pronunciation difficulties</td>
</tr>
<tr>
<td>7</td>
<td>19</td>
<td>FNP, left (1, 1, 3); synkinesia</td>
<td>0</td>
<td>Excessive tear secretion</td>
<td>Definite Motor</td>
<td>Persistent FNP; eye problems</td>
</tr>
<tr>
<td>8</td>
<td>8</td>
<td>FNP, right (1, 1, 4); synkinesia</td>
<td>Pathologic; Romberg's test</td>
<td>Headache; fatigue; neck pain; concentration difficulties</td>
<td>Definite Motor + sensory</td>
<td>Persistent FNP; pain</td>
</tr>
<tr>
<td>9</td>
<td>12</td>
<td>FNP, left (1, 1, 3); synkinesia</td>
<td>Headache; vertigo</td>
<td>Headache</td>
<td>Definite Motor</td>
<td>Persistent FNP; pain</td>
</tr>
<tr>
<td>10</td>
<td>14</td>
<td>FNP, left (1, 1, 3); synkinesia</td>
<td>Headache</td>
<td>Headache</td>
<td>Definite Motor</td>
<td>Persistent FNP; cosmetic problem; poor balance</td>
</tr>
<tr>
<td>11</td>
<td>10</td>
<td>FNP, left (4, 4, 4); synkinesia</td>
<td>Headache; fatigue; neck pain; concentration difficulties</td>
<td>Headache; fatigue; vertigo; weakness in limb</td>
<td>Definite Motor + sensory</td>
<td>Persistent FNP; pain</td>
</tr>
<tr>
<td>12</td>
<td>7</td>
<td>Deviant caloric test</td>
<td>Impaired finger opposition</td>
<td>Headache; vertigo</td>
<td>Definite Motor + sensory</td>
<td>Neuphathy; impaired fine motor skills; poor balance</td>
</tr>
<tr>
<td>13</td>
<td>15</td>
<td>0</td>
<td>Decreased facial sensitivity</td>
<td>Headache</td>
<td>Definite Motor + sensory</td>
<td>Trigeminal neuropathy; pain</td>
</tr>
<tr>
<td>14</td>
<td>12</td>
<td>0</td>
<td>Hyperreflexia in right leg; positive Babinski's sign</td>
<td>Weakness in limb; asymmetric walk; fatigue</td>
<td>Definite Motor + sensory</td>
<td>Hemiarexia; impaired motor skills</td>
</tr>
<tr>
<td>15</td>
<td>11</td>
<td>0</td>
<td>Impaired toe-heel walk; impaired sense of vibration; impaired finger opposition</td>
<td>Problems with writing; numbness in limb</td>
<td>Definite Motor</td>
<td>Trigeminal neuropathy; impaired sensibility; impaired fine motor skills</td>
</tr>
<tr>
<td>16</td>
<td>13</td>
<td>—</td>
<td>Pathologic; Romberg's test; foot drop</td>
<td>Headache; fatigue; vertigo; weakness in limb</td>
<td>Definite Motor</td>
<td>Peripheral nerve palsy; poor balance; pain</td>
</tr>
<tr>
<td>17</td>
<td>15</td>
<td>Head shake nystagmus</td>
<td>0</td>
<td>Neck pain; vertigo</td>
<td>Possible Sensory</td>
<td>Pain; poor balance</td>
</tr>
<tr>
<td>18</td>
<td>16</td>
<td>0</td>
<td>Headache; fatigue; joint pain; numbness in limb</td>
<td>Headache; fatigue; joint pain; numbness in limb</td>
<td>Possible Sensory</td>
<td>Pain; paresthesia</td>
</tr>
<tr>
<td>19</td>
<td>12</td>
<td>Head shake nystagmus</td>
<td>0</td>
<td>Numbness in limbs; vertigo</td>
<td>Possible Sensory</td>
<td>Polyneuropathy; poor balance</td>
</tr>
<tr>
<td>20</td>
<td>19</td>
<td>0</td>
<td>Headache; fatigue; radiant pain in limb; concentration difficulties</td>
<td>Headache; fatigue; radiant pain in limb; concentration difficulties</td>
<td>Possible Sensory</td>
<td>Pain; radiculopathy</td>
</tr>
<tr>
<td>21</td>
<td>9</td>
<td>End position nystagmus</td>
<td>0</td>
<td>Headache; neck pain; vertigo</td>
<td>Possible Sensory</td>
<td>Pain; poor balance</td>
</tr>
<tr>
<td>22</td>
<td>13</td>
<td>0</td>
<td>Headache; facial pain</td>
<td>Headache; facial pain</td>
<td>Possible Sensory</td>
<td>Pain; trigeminal neuropathy</td>
</tr>
<tr>
<td>23</td>
<td>15</td>
<td>0</td>
<td>Headache; fatigue; sensitive to light and sound; concentration difficulties</td>
<td>Headache; fatigue; sensitive to light and sound; concentration difficulties</td>
<td>Possible Sensory</td>
<td>Pain; photophobia and phonophobia</td>
</tr>
</tbody>
</table>

FNP, facial nerve palsy; LNB, Lyme neuroborreliosis; 0, normal.

a Age at follow-up.

b The House-Brackmann grading system for evaluation of facial nerve function in forehead, orbital, and oral area. 1, normal; 2, mild; 3–4, moderate; 5, severe; 6, total loss of function.27
palsy at follow-up, which is slightly more than in previous studies based on
oto-neurologic examination.18–20 It could partly be explained by the risk of bias
due to the expected higher inclination to assign for a re-evaluation, if the
child or the parents (or guardians) experience persistent symptoms. How-
ever, the severity of the persistent facial nerve palsy among our patients
was moderate, which is in line with earlier reports, and no child was found
to have a severe or total loss of facial nerve function. Only 1 child reported
a re-infection of LB with facial nerve palsy at the follow-up, thus sequelae
after a secondary LNB should not have influenced our results. Patients with
persistent facial nerve palsy reported subjective symptoms such as eye-
closing impairment, excessive tear secretion, pronunciation difficulties,
cosmetic complaints, and social problems. Thus, this study confirms that
persistent facial nerve palsy causes facial symptoms that might be problem-
atic to the specific child.

The severity of the facial nerve palsy or
other neurologic deficits in each indi-
vidual patient on admission are not
described in detail in our study because
the clinical examinations on admission
were performed by different physicians
due to the retrospective design and
might for this reason have been less
valid. However, clinical data from
medical records are shown in Table 1
and form the basis in each patient
for whether persistent neurologic
signs and/or symptoms at follow-up
should be defined as sequelae or not
(Table 2).

Objective neurologic findings, such
as persistent neuropathy, trigeminal
neuropathy, hemiparesis after an LNB
associated stroke, polyneuropathy, and
peroneal nerve palsy, were found in
single patients with LNB at follow-up.
These findings correlated well in
character with neurologic signs and
symptoms noted at diagnosis and were
categorized as definite sequelae. Fur-
thermore, neurologic signs and symp-
toms that were less specific, but
correlated well in character and time
after the LNB in the specific patient,
were defined as possible sequelae.
Many of these children with possible
sequelae had neurologic deficits of
sensory character, which are admit-
tedly more difficult to determine at the
neurologic examination than clear
motor deficits. The association to LNB
is consequently more difficult to assess
and therefore the definition of possible
sequelae seems accurate.

Furthermore, we believe it is unlikely
that some of the children would have
had an additional undiagnosed neuro-
logic disease because objective findings
at follow-up were congruent with
findings at diagnosis, and no child
reported a history of major neurologic
symptoms or neurologic disease before
the LNB or during follow-up.

Sensory deficits as sequelae after LNB
in children has been described by Wang
et al,28 who report that numbness or
tingling in limbs was more frequent
among patients with LNB than controls.
Pain, numbness, or a feeling of weak-
ness in limbs were, all taken together,
more often reported by patients with
LNB than controls in our study, and we
believe that these symptoms are cor-
rectly interpreted as sequelae after
LNB. Furthermore, many patients had
a mixed clinical picture of both motor
and sensory deficits, which is interesting
and not previously highlighted in liter-
atue.

Clinical signs of balance nerve dys-
function, such as deviant caloric test,
head shake nystagmus, and prominent
end position nystagmus, were found in
4 children at the follow-up examination.
This could probably be interpreted as
sequelae after an initial affection of the
eighth cranial nerve, in conjunction
with the acute facial nerve palsy. It has
previously been reported that both
pediatric and adult patients with LNB
may experience vertigo on admission.15,19
In our present study, we have shown
that some patients experience vertigo
as a persistent symptom after LNB.
Although vertigo is a nonspecific symp-
tom, it was more frequently reported
by patients with LNB than controls.
Vertigo was also connected to objective
neurologic findings, such as balance
nerve dysfunction in 4 children as
mentioned above, and postural un-
steadiness in 2 children (ie, pathologic
Romberg’s test). Thus, a small group of
children may get a persistent balance
nerve dysfunction after LNB that may
be troublesome for the specific child.
However, whether these children might
have acquired these abnormalities

| TABLE 5 Self-Reported Symptoms in Patients With LNB at Follow-Up and Controls |
|--------------------------------|-----------------|-----------------|-----------------|
| Major Subjective Symptoms*   | Patients With LNB (n = 84), n (%) | Controls (n = 84), n (%) | P |
| Headache                      | 28 (33)          | 32 (38)          | NS             |
| Fatigue                       | 19 (23)          | 29 (34)          | NS             |
| Facial problemsb              | 7 (8)            | 0 (0)            | <.001          |
| Neck pain or stiffness        | 9 (11)           | 5 (6)            | NS             |
| Vertigo                       | 6 (7)            | 1 (1)            | <.001          |
| Pain, numbness, or weakness in limbs | 6 (7)          | 1 (1)            | <.001          |
| Poor appetite or wt loss      | 4 (5)            | 5 (6)            | NS             |
| Memory or concentration problems | 9 (11)          | 5 (6)            | NS             |
| Sleeping disorder             | 10 (12)          | 7 (8)            | NS             |
| Affected daily activities     | 14 (17)          | 12 (14)          | NS             |
| Affected school performance   | 12 (14)          | 8 (10)           | NS             |
| No reported symptoms          | 34 (40)          | 41 (49)          | NS             |

LNB, Lyme neuroborreliosis; NS, nonsignificant.
* Several individuals reported several symptoms.
† Symptoms associated with the persistent facial nerve palsy.
subsequent to their LNB treatment or not is unclear, and results should be interpreted with caution.

Regarding nonspecific subjective symptoms such as headache, fatigue, memory or concentration problems, or sleeping disorders, no differences were found between confirmed patients with LNB and controls in this long-term follow-up study. This is an important finding, which is in line with our previous short-term follow-up study of children with LNB, in which patients with LNB 6-months posttreatment did not report nonspecific subjective symptoms more frequently than controls.15 These results, taken together, help us to understand that nonspecific subjective symptoms after LNB, in the short- and long-term perspective, should not be considered as treatment failure or sequelae after LNB.

Long duration of symptoms before the start of treatment has been connected to a higher rate of persistent neurologic deficits.17 We could not confirm these findings in our present retrospective long-term follow-up study or in a previous prospective study,13 nor did we find other prognostic factors of importance for clinical outcome.

There has been a controversy about the most appropriate therapeutic management in LNB.30 In our present study, patients treated with oral doxycycline did not have a higher rate of sequelae than patients treated with intravenous ceftriaxone or penicillin. Several previous studies revealed that intravenous ceftriaxone has not proven to be superior to oral doxycycline.14,30,31 However, most studies have been conducted in a European setting with all 3 subspecies of *Borrelia burgdorferi sensu lato* as pathogenic agents. In the United States (with *Borrelia burgdorferi sensu stricto* only), the therapeutic tradition has been to use intravenous antibiotics in cases of confirmed LNB.3,32 Thus, prospective multicenter clinical trials in North America are warranted.30,32

Whether persistent symptoms after LNB do affect daily activities or quality of life has been discussed in several studies and is of interest.33–35 We have not included a validated questionnaire for quality of life in our study, but self-reported symptoms did affect daily activities or school performance to the same extent among patients with LNB as controls (23% vs 20%, details in Table 5). These results are in line with a previous study in which both quality of life and neuro-psychiatric tests revealed equal results between children post LB treatment and controls.24

**CONCLUSIONS**

In this study, the long-term clinical recovery rate was 73% in children with confirmed LNB. Persistent facial nerve palsy occurred in 13% of patients, whereas other motor or sensory deficits were found in another 14% of patients, causing impaired fine motor skills, poor balance, or persistent pain. This has not been highlighted in previous studies. However, neurologic deficits after LNB did not seem to affect daily activities and school performance more often among patients than controls and should generally be considered as mild. Furthermore, nonspecific subjective symptoms, such as headache, fatigue, and memory or concentration problems, were reported as often among patients as controls and should not be considered as sequelae after LNB.

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