We describe 5 pediatric cases of Neisseria meningitidis serogroup W135 infection. Infectious and/or reactive extrameningeal involvement was frequent. One patient had a persistent postmeningococcal inflammatory syndrome. Four of 5 isolates belonged to the clonal complex 37. The important risk of extrameningeal complications must be borne in mind when treating children with N. meningitidis W135 infection.

Outbreaks of Neisseria meningitidis serogroup W135 infection were recently reported worldwide [1–4]. In the United States, N. meningitidis W135 accounted for 4% of all N. meningitidis infections between 1992 and 1996 [5]. In 1994, N. meningitidis W135 represented <0.3% of blood isolates referred to the French National Meningococcal Reference Center, but this prevalence increased to 8% between 1999 and 2002 [6]. This increase was related to clonal expansion of N. meningitidis W135 strains belonging to the clonal complex of electrophoretic type 37 (ET-37), responsible for outbreak among pilgrims to Mecca and their contacts in the year 2000 [1, 6].

In the year 2001, N. meningitidis W135 and strains of serogroup A were equally present in children with bacterial meningitis aged 5–15 years at the end of the epidemic season in Burkina Faso and Niger [2]. In France, during the period of January 2000 through August 2003, a total of 14 cases of meningitidis W135 infection were recorded in children aged 2 months to 15 years, and these accounted for 3.1% of the 458 cases of N. meningitidis infection reported to a national pediatric meningitis monitoring network (ACTIV).

No precise data on the clinical manifestations and outcome of these infections in children are available. Therefore, we analyzed the clinical features and strain characteristics of 5 children hospitalized at our institution for N. meningitidis W135 infection.

Patients and methods. During the period of June 2000 through December 2002, 5 children were admitted to Robert Debré Hospital (Paris, France) for N. meningitidis W135 infection. Clinical and biological data were collected retrospectively from the case records. Data on sex, age at diagnosis, and possible infective contacts were recorded. The presenting manifestations, bacteriological diagnosis, secondary sites of infection and/or reactive complications, antimicrobial chemotherapy, outcome, and sequelae were also recorded.

N. meningitidis was isolated by culture of CSF, joint fluid, or blood samples on a chocolate agar plate after 24 h of incubation at 37°C in 5% CO₂. The MICs of penicillin G, amoxicillin, and cefotaxime were determined using the Etest (AB Biodisk) on Mueller-Hinton medium (bioMérieux) after 24 h of incubation at 37°C in 5% CO₂. Serogroup W135 was identified by latex particle agglutination testing using the Slidex meningitis kit (Bio-Rad). Strains belonging to the clonal complex ET-37 were characterized by multilocus sequence typing and multilocus DNA fingerprinting, as described elsewhere [7]. Relatedness of ET-37 strains to the strain of the outbreak of the year 2000 was analyzed by PFGE [7, 8]. Nonculture diagnosis was performed as described elsewhere [9].

Results. Three boys and 2 girls with N. meningitidis W135 infection were admitted to our institution during the period of June 2000 through December 2002. The median age was 34 months (range, 19 months to 11 years; table 1). Only 2 patients (patients 2 and 5) had identifiable contacts with a pilgrim returning from Mecca.

Initial meningeal involvement was found in 3 of the 5 children (patients 1–3), with N. meningitidis W135 recovery from CSF and blood cultures. Two children (patients 2 and 3) had a meningeal syndrome, and 1 child (patient 1) had focal neurological signs (right hemiparesis and right facial paralysis) associated with a right-side uveitis, although brain CT findings were normal. Two children presented with joint involvement: patient 4 had arthritis of the right wrist, the right ankle, and the hallux of the left foot, as well as N. meningitidis W135 recovery from joint fluid.
bacteremia; and patient 5 had right hip involvement, and *N. meningitidis* W135 was isolated from joint fluid and blood cultures. None of the children had purpura fulminans.

Penicillin, amoxicillin, and cefotaxime susceptibility profiles are shown in table 1. Three strains were susceptible to penicillin, and 2 (recovered from patients 1 and 5) had intermediate resistance to penicillin. All of the isolates but one (which was recovered from patient 5) belonged to clonal complex ET-37/ST-11 and were indistinguishable from the strain involved in the Hajj 2000 outbreak. The strain recovered from patient 5 was genetically distinct and belonged to the sequence type ST-2495.

Three children (patients 1, 2, and 4) developed secondary infectious and/or reactive extrameningeal involvement (pericardial in 2 cases and articular in 1 case). Patient 4 had a persistent postmeningococcal inflammatory syndrome.

Patient 1 developed pericardial effusion after 5 days of antimicrobial chemotherapy. The results of PCR for *N. meningitidis* serogroups A, B, C, Y, and W135 were positive for pericardial drainage fluid specimens, but the fluid was contaminated with blood (2500 leukocytes/mm³ and 10⁶ erythrocytes/mm³). Patient 4 developed asymptomatic, afebrile, moderate pericardial effusion on 2 occasions, which were 7 days and 3 months after initial diagnosis. Both episodes resolved with receipt of aspirin (5 mg/kg q.d.). Patient 2 developed arthritis of the right elbow and fever (temperature, 38.5°C) 8 days after initial diagnosis of *N. meningitidis* W135 meningitis and 24 h after the withdrawal of antimicrobial chemotherapy. The results of a joint fluid culture were negative.

The 5 children received cefotaxime (200 mg/kg q.d.) in 3 or 4 intravenous injections for ≥7 days. Patient 1 received cefotaxime combined with ciprofl oxacin (20 mg/kg) in 2 intravenous injections for 10 days, owing to severe initial neurological involvement; no articular complications occurred in this child.

Four of the 5 children were healthy, without sequelae, after a median follow-up duration of 18 months (range, 5–22 months). The 2 children with joint involvement recovered after 6 weeks of antibiotic therapy (7 days of cefotaxime therapy and 5 weeks of oral amoxicillin therapy), although patients 1 and 3 recovered after 21 days and 7 days of therapy with intravenously administered third-generation cephalosporin, respectively. In these 4 children, inflammatory signs resolved after a median of 10 days (range, 7–30 days).

Eighteen months after diagnosis, patient 4 was free of pericarditis and had normal physical findings. However, an inflammatory syndrome persisted, with an erythrocyte sedimentation rate of 20–40 mm/h and a platelet count of >500,000 platelets/mm³, requiring treatment with aspirin (5 mg/kg q.d.).

**Discussion.** Few clinical data are available on *N. meningitidis* W135 infection in children. Four of our 5 patients had extrameningeal involvement, affecting the joints (n = 3), pericardium (n = 2), or eyes (n = 1). These complications could be separated into 2 categories: infectious and reactive extrameningeal involvement. Among the 4 children, only 1 (patient 5) clearly had infectious extrameningeal involvement. Delayed pericarditis in patient 1, delayed arthritis in patient 2, and relapsing pericarditis and prolonged inflammatory syndrome in patient 4 are rather indicative of reactive complications. Finally, it was not possible to determine whether the initial uveitis in patient 1 and the small joint arthritis in patient 4 were due to infectious involvement or a reactive mechanism, owing to sampling difficulties.

Apart from sepsis, only a few cases of infectious extrameningeal involvement have been reported in patients with *N. meningitidis* W135 infection. In a series of 4 pediatric cases of *N. meningitidis* W135 infection, there were 2 cases of septicemia, 1 case of meningitis, and 1 case of purpura fulminans, but no infectious extrameningeal involvement was reported [10]. Only a few pediatric cases of articular or pericardial infectious involvement have been reported [11–13].

In a large epidemiological study conducted in the United States from 1992 through 1996, the frequency of arthritis due to all serogroups of *N. meningitidis* was 2% and that of pericarditis was 0.1%, but no prevalent serogroup was described in these extrameningeal complications [5]. Recently, Vienne et al. [14] showed that serogroup W135 was, interestingly, more often isolated from patients with joint infection than were other meningitic isolates.

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**Table 1. Clinical features, strain characteristics, and outcomes for children with *Neisseria meningitidis* W135 infection.**

<table>
<thead>
<tr>
<th>Patient</th>
<th>Sex/age, months</th>
<th>Initial presentation</th>
<th>Secondary complications</th>
<th>MIC, µg/mL*</th>
<th>Clonal complexb</th>
<th>Comments (duration of follow-up, months)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>M/19</td>
<td>Meningitis uveitis</td>
<td>Pericarditis</td>
<td>0.190</td>
<td>0.190</td>
<td>0.023 ET-37/ST-11 Recovery without sequelae (10)</td>
</tr>
<tr>
<td>2</td>
<td>F/48</td>
<td>Meningitis</td>
<td>Arthritis</td>
<td>0.094</td>
<td>0.094</td>
<td>0.08 ET-37/ST-11 Recovery without sequelae (19)</td>
</tr>
<tr>
<td>3</td>
<td>M/24</td>
<td>Meningitis</td>
<td>No</td>
<td>0.094</td>
<td>0.094</td>
<td>0.012 ET-37/ST-11 Recovery without sequelae (22)</td>
</tr>
<tr>
<td>4</td>
<td>M/132</td>
<td>Polyarthritis</td>
<td>Recurrent pericarditis, persistent inflammatory syndrome</td>
<td>0.094</td>
<td>0.125</td>
<td>0.012 ET-37/ST-11 Inflammatory syndrome present (18)</td>
</tr>
<tr>
<td>5</td>
<td>F/22</td>
<td>Monoarthritis</td>
<td>No</td>
<td>0.125</td>
<td>0.125</td>
<td>0.016 ST-2495 Recovery without sequelae (5)</td>
</tr>
</tbody>
</table>

* Determined by molecular genotyping based on multilocus sequence typing, as described elsewhere [7].

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**Notes:**
- *C. microbium* W135 was isolated from joint fluid and blood cultures.
- Patient 1 developed pericardial effusion after 5 days of antimicrobial chemotherapy.
- The 5 children received cefotaxime (200 mg/kg q.d.) in 3 or 4 intravenous injections for ≥7 days.
- Patient 1 received cefotaxime combined with ciprofloxacin (20 mg/kg) in 2 intravenous injections for 10 days, owing to severe initial neurological involvement; no articular complications occurred in this child.
- Four of the 5 children were healthy, without sequelae, after a median follow-up duration of 18 months (range, 5–22 months).
- The 2 children with joint involvement recovered after 6 weeks of antibiotic therapy (7 days of cefotaxime therapy and 5 weeks of oral amoxicillin therapy), although patients 1 and 3 recovered after 21 days and 7 days of therapy with intravenously administered third-generation cephalosporin, respectively.
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N. meningitidis involvement in children infected with 3 of the 5 patients (patients 1, 2, and 4) had reactive extrameningeal involvement. These complications occur generally in the subacute phase of meningococcal disease, 4–10 days after the initiation of antimicrobial treatment. The frequency of such complications seemed to be higher in our series, because 3 of the 5 patients (patients 1, 2, and 4) had reactive extrameningeal involvement. This high frequency of extrameningeal involvement in children infected with N. meningitidis W135 could point to a pathophysiologic mechanism specific to this serogroup.

Four of our 5 patients were infected with N. meningitidis W135 strains belonging to clonal complex ET-37 and indistinguishable from the strain from the Hajj 2000 outbreak. This genotype is overrepresented among serogroup W135 strains, relative to other N. meningitidis serogroups [14]. It has also been implicated in most cases of infectious arthritis due to N. meningitidis serogroup C [14]. Further studies are needed to demonstrate its precise role in infectious and/or reactive extrameningeal involvement linked to N. meningitidis W135 infection.

Only 1 of the 5 children (patient 4) in our series developed sequelae, in keeping with a reported frequency of 11%–19% after N. meningitidis infection [16]. The inflammatory syndrome that persisted 18 months after initial diagnosis may have been a postmeningococcal syndrome, which is rare after N. meningitidis infection. Its pathophysiologic could involve immunooallergic reactions with immune complex, as previously discussed. However, the long duration of this persistent inflammatory syndrome is unusual, compared with reports from other studies [15].

In conclusion, this study shows a particularly high frequency of infectious and, especially, reactive extrameningeal involvement in children infected with N. meningitidis W135. This calls for thorough investigations, both at the time of diagnosis and early during the follow-up period, to identify such complications. The high frequency of genotype ET-37 among N. meningitidis W135 strains could account for extrameningeal and/or reactive complications. However, because the number of patients in the study is low, prospective multicenter studies are needed to determine the frequency, clinical features, and outcome of N. meningitidis W135 infection relative to other N. meningitidis strains. This could help to identify pathogenic factors specific to N. meningitidis W135.

References