Increased Diagnosis of Lemierre Syndrome and Other *Fusobacterium necrophorum* Infections at a Children’s Hospital

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ABSTRACT. Objective. To assess the apparent increase in the diagnosis of Lemierre syndrome (LS) and other *Fusobacterium necrophorum* infections at a large children’s hospital. Infections with *F necrophorum* ranged from peritonsillar abscess to potentially fatal LS. LS is an oropharyngeal infection characterized by septic thrombophlebitis of head and neck veins, complicated by dissemination of septic emboli to pulmonary and systemic sites.

Methods. Review of the medical and laboratory records was conducted of all patients who were seen at or admitted to the Children’s Hospital of Wisconsin with the diagnosis of LS and/or isolation of *F necrophorum* from a clinical specimen between January 1995 and January 2002.

Results. During the 7-year period of the study, there was an increase in the isolation of *F necrophorum* from patients who were seen at Children’s Hospital of Wisconsin, as well as the number of cases of LS. There was 1 isolation of *F necrophorum* from clinical specimens per year from 1996 to 1999, which increased to 10 isolates of the organism from January 2000 to January 2002. During the most recent period, January 2001–January 2002, 5 cases of LS were diagnosed, a distinctive entity not recognized previously at the institution.

Conclusions. The cause for the recent increase in the number of serious infections caused by *F necrophorum* infection diagnosed at our institution is unclear but does not seem to be related to changes in microbiologic techniques or patient demography. We speculate that it could be attributable, in part, to alterations in antibiotic usage patterns in our region. Clinicians need to be aware of the increasing clinical importance of *F necrophorum* infections and the life-threatening nature of LS. *PEDIATRICS* 2003;112:e380–e385. URL: http://www.pediatrics.org/cgi/content/full/112/5/e380; *Fusobacterium necrophorum, Lemierre syndrome, peritonsillar abscess, thrombophlebitis, pulmonary emboli.*

ABBREVIATIONS. LS, Lemierre syndrome; CHW, Children’s Hospital of Wisconsin; CT, computed tomography; WBC, white blood cell; CMV, cytomegalovirus; IgM, immunoglobulin M; EBV, Epstein-Barr virus; WARN, Wisconsin Antibiotic Resistance Network.

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Fusobacterium necrophorum, a Gram-negative, non–spore-forming, obligate anaerobe, is part of the normal flora of the oral cavity, alimentary tract, and female genital tract.1–4 The spectrum of disease associated with this organism ranges from uncomplicated pharyngitis to Lemierre syndrome (LS), an aggressive oropharyngeal infection consisting of pharyngitis, bacteremia, and suppurrative thrombophlebitis, often complicated by metastatic septic emboli.5–11 Since the advent of antibiotic therapy, LS and bacteremia with *F necrophorum* have become rare entities. Consequently, LS has been called the “forgotten disease.”12–15 Within a 12-month period, we treated 5 children at the Children’s Hospital of Wisconsin (CHW) with LS. Therefore, we reviewed microbiology laboratory and hospital records at our institution from January 1995 to January 2002 searching for other cases of *F necrophorum* infection and LS.

METHODS

Approval was obtained from the Institutional Review Board of CHW to review laboratory and medical records of cases of “*Fusobacterium*” and “*F necrophorum*” infection, as well as “Lemierre syndrome.” CHW is a 222-bed hospital located in Milwaukee, Wisconsin. During the study period 1995–2001, CHW had a total of 124 000 inpatient admissions.

The microbiology laboratory identified *F necrophorum* in clinical specimens from a variety of sources from 14 patients between January 1995 and January 2002. Review of Infectious Diseases Section records for the diagnosis of “Lemierre syndrome” revealed an additional case that was not identified in the laboratory search. There was no record of a case of LS at the institution before 2001. In this study, LS was defined as signs and symptoms of oropharyngeal infection associated with systemic manifestations, including fever, evidence of hemodynamic instability, clinical or radiologic evidence of cervical venous thrombophlebitis, and documentation of *F necrophorum* bacteremia and/or evidence of invasive cervical infection.

RESULTS

Fourteen cases of confirmed *F necrophorum* infection were seen at CHW between January 1995 and January 2002 (Table 1). One other patient (patient 14) had a clinical diagnosis of LS, although her blood culture remained negative, presumably as a result of previous antibiotic therapy for painful cervical swelling and odynophagia of 1 week’s duration. A computed tomography (CT) scan of this patient’s neck revealed thrombophlebitis of the left internal jugular vein.

All patients recovered fully. Five of the 15 patients had LS, and 8 had peritonsillar abscesses. Two patients did not fit into either category. Patient 4 was
Table 1. Fusobacterium necrophorum Infections at CHW, January 1995–January 2002

<table>
<thead>
<tr>
<th>Patient</th>
<th>Year</th>
<th>Age/Sex (Years)</th>
<th>Previous Antibiotics</th>
<th>Isolate Source</th>
<th>Clinical Diagnosis</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>1996</td>
<td>15/M</td>
<td>Y</td>
<td>PAF</td>
<td>Peritonsillar abscess</td>
</tr>
<tr>
<td>2</td>
<td>1997</td>
<td>14/F</td>
<td>Y</td>
<td>PAF</td>
<td>Peritonsillar abscess</td>
</tr>
<tr>
<td>3</td>
<td>1998</td>
<td>13/F</td>
<td>Y</td>
<td>PAF</td>
<td>Peritonsillar abscess</td>
</tr>
<tr>
<td>4</td>
<td>1999</td>
<td>16/F</td>
<td>N</td>
<td>BAL</td>
<td>Systemic HSP</td>
</tr>
<tr>
<td>5</td>
<td>2000</td>
<td>7/M</td>
<td>N</td>
<td>Blood</td>
<td>Streptococcal pharyngitis</td>
</tr>
<tr>
<td>6</td>
<td>2000</td>
<td>16/F</td>
<td>Y</td>
<td>PAF</td>
<td>Peritonsillar abscess</td>
</tr>
<tr>
<td>7</td>
<td>2000</td>
<td>17/F</td>
<td>N</td>
<td>PAF</td>
<td>Peritonsillar abscess</td>
</tr>
<tr>
<td>8</td>
<td>2000</td>
<td>18/F</td>
<td>Y</td>
<td>PAF</td>
<td>Peritonsillar abscess</td>
</tr>
<tr>
<td>9</td>
<td>2000</td>
<td>15/F</td>
<td>N</td>
<td>PAF</td>
<td>Peritonsillar abscess</td>
</tr>
<tr>
<td>10</td>
<td>2001</td>
<td>16/M</td>
<td>N</td>
<td>Blood</td>
<td>LS</td>
</tr>
<tr>
<td>11</td>
<td>2001</td>
<td>16/M</td>
<td>N</td>
<td>PAF</td>
<td>Peritonsillar abscess</td>
</tr>
<tr>
<td>12</td>
<td>2001</td>
<td>17/M</td>
<td>N</td>
<td>Blood</td>
<td>LS</td>
</tr>
<tr>
<td>13</td>
<td>2001</td>
<td>18/F</td>
<td>N</td>
<td>Blood</td>
<td>LS</td>
</tr>
<tr>
<td>14</td>
<td>2001</td>
<td>14/F</td>
<td>Y</td>
<td>NA</td>
<td>LS</td>
</tr>
<tr>
<td>15</td>
<td>2002</td>
<td>17/F</td>
<td>N</td>
<td>Blood, skin lesion</td>
<td>LS</td>
</tr>
</tbody>
</table>

PAF indicates peritonsillar abscess fluid; BAL, bronchial-alveolar lavage; HSP, Henoch Schonlein purpura.

Transported from an outside institution with cardio-pulmonary decompensation and was found to have pulmonary hemorrhage at bronchoscopy and glomerulonephritis on renal biopsy. She received a diagnosis of Henoch Schonlein purpura. Blood cultures showed no growth, but she had pure positive culture for *F necrophorum* from a bronchial-alveolar lavage, of unknown clinical significance. Patient 5 was never hospitalized but seen in the emergency department for a febrile illness. Initially believed to have a viral syndrome, the patient was reevaluated after his blood culture demonstrated a Gram-negative bacillus, identified as *F necrophorum*. A throat culture was also positive for group A β-hemolytic streptococcus. On recall, he had become afebrile without antibiotic treatment. A repeat blood culture was obtained, which was sterile, and the patient was treated with orally administered penicillin.

Ten of 14 of the cases of laboratory-confirmed *F necrophorum* infection occurred during the last 2 years of data analysis (February 2000–January 2002), and all of the cases of LS occurred during the last year of the study. All of the patients except 1 were teenagers. There was a 2:1 ratio of affected girls to boys. During the period of the study, there were no significant changes in the general demography or number of patients admitted to CHW. There were no changes in microbiologic technique that should have affected isolation or identification of the organism.

Six of the patients were receiving oral antibiotics at the time of presentation to the hospital, including 5 of 8 of the patients with *F necrophorum* peritonsillar abscesses and 1 of 5 patients with LS. In the 5 patients in whom *F necrophorum* was cultured from blood, it was the only organism isolated. No patient who was receiving antibiotics grew *F necrophorum* from blood culture, even those who had had positive blood cultures before the initiation of antibiotic therapy. In this series, no patient had a second positive blood culture, presumably because of early institution of antibiotic therapy. In 4 of the 8 patients with peritonsillar abscesses in whom *F necrophorum* was isolated, other organisms, generally mouth flora such as the *Streptococcus viridans* group and *Staphylococcus epidermidis*, were isolated. Although formal antibiotic susceptibility testing was not performed, all *F necrophorum* isolates were β-lactamase negative.

Other than 2 patients with hemoglobin SC disease (patients 5 and 6), all 15 patients were healthy and without significant medical problems requiring previous hospitalization before the onset of *F necrophorum* infection. None had had significant infection previously. Duration of symptoms did not significantly differ between the patients with peritonsillar abscesses and LS. Advancing oropharyngeal disease, manifested as cervical swelling, was seen in 4 of 8 of the patients with peritonsillar abscesses.

Although all 5 of our patients with LS initially complained of severe pharyngitis, their chief complaint or the reason for seeking medical care was not always a “sore throat” (Table 2). Vomiting was the chief complaint in 3 of the 5 patients. Other frequent complaints included prolonged pharyngitis, cervical swelling, abdominal pain, fatigue/lethargy, fever/chills, and weight loss. Four of the 5 had physical findings of right upper quadrant pain and/or hepatomegaly. Evidence of metastatic infection was seen in 3 of the 5 patients with LS. Organ systems affected by septic emboli included lungs (3 patients), liver, bones, and skin. Three patients received anticoagulant therapy.

Four of 5 of the patients with LS presented to the emergency department with evidence of shock based on changes in vital signs and physical examination. Of note, the 1 patient with LS who did not present in shock (patient 14) had been treated with oral antibiotics as an outpatient before hospitalization. Two patients presented with evidence of pulmonary involvement as indicated by tachypnea and hypoxia. A third patient (patient 10) with radiologic evidence of pulmonary septic emboli remained asymptomatic. Common physical examination findings included “toxicity,” dehydration, pharyngitis, painful cervical swelling, and right upper quadrant abdominal pain. Two patients had hepatosplenomegaly on physical examination.

The range of the white blood cell (WBC) count in the patients with evidence of shock on presentation was 380-381.
### TABLE 2. LS: Clinical Findings

<table>
<thead>
<tr>
<th>Patient</th>
<th>Symptom Duration Before Hospitalization</th>
<th>Presenting Complaints</th>
<th>Associated Complaints</th>
<th>Parenteral Antibiotic Therapy</th>
<th>Anticoagulation</th>
<th>Complications</th>
</tr>
</thead>
<tbody>
<tr>
<td>10</td>
<td>8 d</td>
<td>Vomiting/diarrhea</td>
<td>Pharyngitis, weight loss, fever, shoulder, elbow, knee pain, fatigue</td>
<td>Clindamycin (8 wk)</td>
<td>–</td>
<td>Septic pulmonary emboli, multifocal osteomyelitis (elbow, both shoulders and knees), thrombocytopenia, external jugular vein thrombophlebitis</td>
</tr>
<tr>
<td>12</td>
<td>2 wk</td>
<td>Abdominal pain/vomiting</td>
<td>Pharyngitis, cervical pain, weight loss, fever, fatigue</td>
<td>Ampicillin/sulbactam (4 wk)</td>
<td>–</td>
<td>Periadrenal edema</td>
</tr>
<tr>
<td>13</td>
<td>10 d</td>
<td>Pharyngitis/vomiting/diarrhea</td>
<td>Cervical swelling, abdominal pain, fever, chest pain, myalgia, fatigue</td>
<td>Piperacillin/tazobactam and Metronidazole (4 wk)</td>
<td>+</td>
<td>Septic pulmonary emboli; thrombocytopenia, cholangitis</td>
</tr>
<tr>
<td>14</td>
<td>6 d</td>
<td>Cervical swelling</td>
<td>Pharyngitis</td>
<td>Ampicillin/sulbactam (4 wk) then ampicillin/sulbactam (5 wk)</td>
<td>+</td>
<td>Internal jugular thrombophlebitis</td>
</tr>
<tr>
<td>15</td>
<td>2 wk</td>
<td>Pharyngitis</td>
<td>Cervical pain and swelling, dyspnea, fever, chest and back pain, weight loss, lethargy, pustular rash</td>
<td>Ampicillin/sulbactam and clindamycin (1 wk) then ampicillin/sulbactam (5 wk)</td>
<td>+</td>
<td>Septic pulmonary and skin emboli thrombocytopenia; cervical thrombophlebitis</td>
</tr>
</tbody>
</table>

### TABLE 3. LS: Laboratory Findings

<table>
<thead>
<tr>
<th>Patient</th>
<th>Peak WBC (4–12 × 10^9/μL)</th>
<th>Lowest Platelet Count (150–450 × 10^3 μL)</th>
<th>Peak ALT/Total Bilirubin (5–35 IU/L/0.0–1.2 mg/dL)</th>
<th>Lowest Albumin (3.8–5.4 g/dL)</th>
<th>Peak BUN/CR (5–20 mg/dL/0.1–1.2 mg/dL)</th>
<th>Coagulation Studies</th>
<th>Peak ESR/CRP (0–20 mm/h/0.1 mg/dL)</th>
<th>Serologic Studies</th>
</tr>
</thead>
<tbody>
<tr>
<td>10</td>
<td>11.4</td>
<td>55</td>
<td>49/13</td>
<td>2.5</td>
<td>39/1.3</td>
<td>PTT = 33.5 sec, fibrinogen = 419 mg/dL, Ddimer = 4.0–0.08 μg/mL</td>
<td>13/14.3</td>
<td>Positive: Monospot, EBV IgM and IgG Negative: ASO</td>
</tr>
<tr>
<td>12</td>
<td>17.9</td>
<td>234</td>
<td>14/12</td>
<td>3.8</td>
<td>9/.7</td>
<td>PTT = 31 sec, fibrinogen = 507 mg/dL, Ddimer = 4.0–0.05 μg/mL</td>
<td>ND/ND</td>
<td>ND</td>
</tr>
<tr>
<td>13</td>
<td>50</td>
<td>29</td>
<td>33/123</td>
<td>2</td>
<td>107/3</td>
<td>PTT = 33.4 sec, fibrinogen = 498 mg/dL, Ddimer = 1.6–32 μg/mL</td>
<td>100/9</td>
<td>Positive: CMV IgM Negative: ASO, EBV IgM and IgG, CMV IgG</td>
</tr>
<tr>
<td>14</td>
<td>4.9</td>
<td>ND/ND</td>
<td>ND</td>
<td>ND</td>
<td>ND</td>
<td>PTT = 29.1 sec, fibrinogen = 457 mg/dL, Ddimer ≤ 0.2 μg/mL</td>
<td>66/1.3</td>
<td>Positive: EBV IgG and IgM, CMV IgM Negative: ASO, monospot</td>
</tr>
<tr>
<td>15</td>
<td>26.4</td>
<td>9</td>
<td>22/22</td>
<td>2.2</td>
<td>37/.9</td>
<td>PTT = 28.2 sec, fibrinogen = 694 mg/dL, Ddimer = 0.2 μL</td>
<td>42/23.6</td>
<td>Positive: ASO, EBV IgG Negative: EBV IgM, CMV IgM</td>
</tr>
</tbody>
</table>

ND indicates not done; ASO, antistreptolysin O titer.
was 11.4 to 50 × 10^3 WBC/µL with a left shift on the differential (Table 3). Patient 14, who was treated with antibiotics before hospitalization, had a normal blood cell count of 4.9 × 10^3 WBC/µL and a normal differential on blood smear. Three of 5 patients were thrombocytopenic on presentation. Of the 4 patients evaluated, only 1 had evidence of more than minimal liver chemistries abnormalities along with an increase in bilirubin to 12.3 mg/dL. A transvenous liver biopsy obtained in patient 13 demonstrated nonspecific triaditis of the intrahepatic biliary system. None of the patients had evidence of disseminated intravascular coagulation. Four of 5 (the other patient did not have erythrocyte sedimentation rate or C-reactive protein measured) had evidence of systemic inflammation based on elevated C-reactive protein (range: 1.3–23.6 mg/dL). None of the patients had detailed immune evaluation after their infection.

There was evidence of simultaneous co-infection, reactivation, or polyclonal antibody stimulation in all 4 of the patients with LS who were so evaluated. One patient had an elevated antistreptolysin O titer, 1 patient had a positive cytomegalovirus (CMV) immunoglobulin M (IgM) titer, 1 patient had a positive Epstein-Barr virus (EBV) IgM titer, and another patient had elevated IgM titers to both CMV and EBV.

Radiologic data were obtained in all 5 LS patients using ultrasound, CT, magnetic resonance imaging, and nuclear medicine techniques. Three patients had unequivocal evidence of venous thrombosis (1 each in the internal jugular, external jugular, and anterior neck veins; Fig 1). Three had evidence of bilateral septic pulmonary emboli. Although 1 patient (patient 14) with jugular venous thrombosis had no signs of pulmonary involvement, another patient (patient 13) with radiographic findings consistent with multiple pulmonary emboli (Fig 2) could not be demonstrated to have a defined venous thrombosis in the neck. One patient (patient 10) had evidence of multifocal osteomyelitis (right elbow, bilateral shoulders, and bilateral knees).

All of our patients with LS recovered completely. The median length of hospitalization was 9 days with a range of 5 to 14 days, compared with the patients with peritonsillar abscesses, who had hospital stays in the range of 1 to 3 days. All patients with LS were treated for 4 to 6 weeks with parenterally administered antibiotics, with the exception of patient 10, whose course was complicated by multifocal osteomyelitis and who was treated for a total of 8 weeks.

DISCUSSION

From the time of its initial description until the dawn of the antibiotic era in the 1940s, >250 cases of F necrophorum bacteremia were reported worldwide.11,16 However, after the inception of the widespread use of oral antibiotics for actual and presumed streptococcal pharyngitis between 1950 and 1972, Bartlett and Finegold were17 unable to identify in the medical literature the report of a single case of LS. In 1995, Leugers and Clover18 were able to find 40 cases of LS reported between 1950 and 1995, with all but 2 of the cases occurring during the last 2 decades (1980s–1990s) of his study. The incidence of F necrophorum septicemia and LS in Denmark from 1990 to 1995 was reported as 1.5 and 0.8 per million people per year, respectively. In the 49 cases that these authors identified, there was a doubling of the number of cases in the later years of their analysis, 16 cases in the first 3 years and 33 cases during the last 3 years.19

During the period of the current review January 1995 to January 2002, there were 14 cases of confirmed infections caused by F necrophorum and an additional clinically diagnosed case at CHW. Most of the infections occurred during the last 2 study years. We were able to categorize the majority of the patients into 2 groups: those with uncomplicated peritonsillar abscesses and those with LS. It is evident that F necrophorum causes a spectrum of disease in children ranging from peritonsillar/peritonsillar abscess to full-blown LS.

Laboratory data in our patients with LS frequently showed a marked leukocytosis (up to 50 000) with a left shift on blood smear. Thrombocytopenia (as low as 9000) was present in 3 of the 5 patients. This was presumed to be secondary to consumptive coagulopathy, but this could not be confirmed by coagulation studies. This finding may be related instead to bacterial platelet aggregation factors associated with Fusobacteria.2,11,20,21

Of note was evidence of simultaneous or preexistent infections in all 4 of our LS patients in whom such evidence was sought. Infectious agents included Streptococcus pyogenes, CMV, and EBV. In
1984, Portman et al reviewed the occurrence of peritonsillar abscess complicating infectious mononucleosis. They found that 20% of patients who were hospitalized for peritonsillar abscess were also found to have evidence of concurrent EBV infection. There have been 2 previous reports, totaling 4 cases, demonstrating an association of LS with infectious mononucleosis. Two of our patients also seemed to have active EBV infection around the time of diagnosis of LS.

Classically, LS is characterized by thrombophlebitis of the internal jugular vein. However, thrombophlebitis can occur in a variety of vessels in the head and the neck, including the pharyngeal venous plexus and the peritonsillar veins. LS also has been associated with cavernous sinus thrombosis and lateral sinus thrombosis. Three of our patients with LS had definitive radiologic evidence of thrombophlebitis in the jugular system. However, thrombophlebitis is not always documented despite suggestive clinical manifestations, as evident in patient 13, who developed pulmonary emboli but lacked a detectable thrombosed cervical vessel. When jugular thrombophlebitis does occur, septic thromboemboli are often the result, most commonly to the lungs as seen in 3 of our patients. Less commonly metastatic infection can be seen in the systemic circulation resulting in hepatic, osseous, and cutaneous emboli as noted in 3 of our patients.

In the preantibiotic era, LS had a mortality rate as high as 90%. Since the advent of antibiotic therapy, the mortality rate has decreased to <20%. Successful treatment of patients with LS involves administration of parental antibiotics active against _F. necrophorum_. _F. necrophorum_ is an anaerobe, usually susceptible to penicillin, clindamycin, metronidazole, and chloramphenicol. Susceptibility to cephalosporins, erythromycin, and tetracyclines is variable. This organism is resistant to aztreonam and trimethoprim-sulfamethoxazole, as well as aminoglycosides. Penicillin treatment failures of LS have been reported, which are presumed to be caused by _β_-lactamase production of the infecting microorganism. In 1990, Appelbaum et al found 40% of _Fusobacteria_ isolates to elaborate _β_-lactamase. Of these, _F. nucleatum_ and _F. necrophorum_ accounted for >40% of _β_-lactamase producers. Therefore, most experts recommend the use of _β_-lactamase-resistant antibiotics with anaerobic activity such as intravenous ticarcillin-clavulanate, ampicillin-sulbactam, metronidazole, or clindamycin.

In addition to antibiotic therapy, surgical drainage of abscesses and debridement of necrotic tissue may be indicated. When considering the spectrum of disease caused by _F. necrophorum_, early surgical intervention may prevent the development of LS. In our analysis, 4 of the 8 patients with peritonsillar abscesses presented with cervical swelling and were treated with tonsillectomy and short-course antibiotic therapy. None of these patients progressed to the development of LS. In the preantibiotic era, LS was frequently treated with ligation of thrombosed vessels, especially the internal jugular vein. With the use of parental antibiotic therapy, ligation of the internal jugular vein is now rarely indicated.

The role of anticoagulation therapy in LS remains controversial. Advocates of systemic anticoagulation cite the potential for faster resolution of the thrombophlebitis and bacteremia, limiting the development of new metastatic foci. Controlled studies that assess the value of anticoagulation in thrombophlebitis of the jugular venous system have not been conducted.

Since the advent of antibiotic therapy, LS has become exceedingly rare and has been called the “forgotten disease.” Recently, there has been an increase in reports of sporadic cases of LS. At our institution, we have seen a marked increase in the diagnosis of this unusual condition. The cause of this apparent increase is uncertain. Our laboratory has not changed relevant microbiologic techniques for culturing anaerobes in >15 years. We have not seen an increased rate of isolation of other anaerobes. It is possible that we have become more proficient in our ability to diagnose this syndrome as a result of our recent experi-

Fig 2. Computed axial contrast image of the upper chest of patient 13. The image demonstrates multiple pulmonary nodules and a small loculated pleural effusion on the right.

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ence with the entity. However, the clinical syndrome is so distinctive and the pathogen so unusual that it seems unlikely that it would have been missed previously. The same infectious disease physicians and radiologists who are making the diagnosis now have been at the institution for >20 years but failed to diagnose it previously.

The increase in LS could also be attributable to the increasingly judicious use of antibiotics in Wisconsin or a change in the antibiotic susceptibility pattern of the organism. A recent publication by Belongia et al demonstrated that multifaceted education programs for clinicians and parents led to an overall decrease in antibiotic prescriptions of approximately 20% in northern Wisconsin between 1997 and 1998. As a result of this work, the Wisconsin Antibiotic Resistance Network (WARN; http://www.wisconsinmedicalsociety.org/WARN) was developed and a statewide health education campaign was begun in 1999 to educate the public and clinicians about appropriate antibiotic use for upper respiratory infections and to reduce the prevalence of antibiotic-resistant bacteria. The increase in the number of patients infected with *F necrophorum* occurred during the last 2 of the 7 years that were analyzed in our study, 1 year after the initiation of the WARN campaign. A component of WARN’s campaign is to decrease antibiotic use for pharyngitis that is culture negative for group A streptococcus. As a result, it is possible that some Wisconsin clinicians may have decreased their prescription of antibiotics for unconfirmed streptococcal pharyngitis. Similarly, there has recently been a marked reduction in the usage of oral antibiotics in children nationwide. In addition, there has been a shift in prescription practices over the past few years away from pharmaceuticals requiring multiple doses daily to those requiring single-or twice-daily dose use. These agents include macrolides such as azithromycin and various second- and third-generation cephalosporins, which lack activity against *F necrophorum*. As physicians become more diligent in the selective use of antibiotic agents for well-documented streptococcal pharyngitis and turn away from the use of traditional antibiotics such as penicillin and amoxicillin to agents inactive against *F necrophorum*, it is possible that there will be an additional increase in the number of *F necrophorum* infections, as noted during the preantibiotic era.

REFERENCES

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