Meningitis and pneumonia in Guatemalan children: the importance of *Haemophilus influenzae* type b and *Streptococcus pneumoniae*

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ABSTRACT

Objective. *To determine the epidemiology of* Haemophilus influenzae *type b (Hib) and* Streptococcus pneumoniae *invasive infections in hospitalized Guatemalan children. This is an important issue since Hib vaccine has not been incorporated into the routine immunization program in Guatemala and information from hospital records in 1995 indicated a low incidence of Hib and* S. pneumoniae *as causes of meningitis and invasive infections.*

Methods. *Children who were hospitalized in Guatemala City with clinical signs compatible with bacterial infections were evaluated for evidence of Hib or* S. pneumoniae *infection. Normally sterile body fluids were cultured, and antigen detection was performed on cerebrospinal fluid (CSF) and pleural fluid.*

Results. *Of 1 203 children 1–59 months of age hospitalized over a 28-month period, 725 of them (60.3%) had a primary diagnosis of pneumonia, 357 (29.7%) of meningitis, 60 (5.0%) of cellulitis, and 61 (5.1%) of sepsis and other conditions. Hib was identified in 20.0% of children with meningitis and* S. pneumoniae *in 12.9%. The average annual incidence of Hib meningitis was 13.8 cases per 100 000 children under 5 years of age, and 32.4% of meningitides caused by Hib and 58.7% of* S. pneumoniae *meningitides occurred prior to 6 months of age. Case fatality rates were 14.1%, 37.0%, and 18.0%, respectively, for children with Hib,* S. pneumoniae, *and culture-negative and antigen-negative meningitis. Prior antibiotic therapy was common and was associated with significant reductions in CSF–culture–positive results for children with other evidence of Hib or* S. pneumoniae *meningitis.*

Conclusions. *Improvements in case detection, culture methods, and latex agglutination for antigen detection in CSF resulted in identification of Hib and* S. pneumoniae *as important causes of severe disease in Guatemalan children. Using a cutoff of > 10 white blood cells per cubic millimeter in CSF would improve the sensitivity for detection of bacterial meningitis and help estimate the burden of bacterial meningitis in Guatemala and other developing countries.*

Key words *Haemophilus influenzae* type b; meningitis, *Haemophilus*; *Streptococcus pneumoniae*; vaccination; Guatemala.

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In many industrialized countries the incidence of invasive disease caused by *Haemophilus influenzae* type b (Hib) decreased dramatically following widespread use of Hib conjugate vaccines (1–5). Before these vaccines were available, an estimated one in 200 children in the United States of America developed invasive Hib disease before 5 years of age (1). Information from a limited number of developing countries in Africa, Asia, and Latin America indicates that Hib is an important cause of childhood morbidity and mortality, responsible for 25%–65% of bacterial meningitis as well as 15%–25% of severe pneumonia in some areas (4–9). Case fatality rates for meningitis in developing countries are often higher than reported in developed countries because of delays in diagnosis and suboptimal antimicrobial therapy (4, 10–13). Conjugate vaccines offer the potential for preventing these important causes of morbidity and mortality, but the importance of Hib and *Streptococcus pneumoniae* is often underappreciated due to failure to obtain cultures from sick children and suboptimal microbiologic methods. Introduction of Hib vaccines in developing countries like Guatemala has progressed slowly, despite evidence of its effectiveness. Decision makers in developing countries need data before committing limited resources for the purchase of relatively expensive vaccines. Since Hib vaccine had not been incorporated into the public routine immunization program in Guatemala, we initiated a surveillance program to detect invasive diseases caused by Hib and *S. pneumoniae* in order to estimate the burden of severe disease in children in Guatemala City.

METHODS

Study population

Between 1 October 1996 and 31 January 1999 we evaluated children 1 to 59 months of age admitted with clinical signs compatible with bacterial infections to the three major referral hospitals in Guatemala City. We prospectively determined the proportion of infections caused by Hib and *S. pneumoniae*. The three hospitals—Hospital General San Juan de Dios, Hospital Roosevelt, and Hospital General del Instituto Guatemalteco de Seguridad Social (IGSS) (*Spanish name*)—capture approximately 85% of Guatemala City children hospitalized with meningitis. Private hospitals and sanatoriums serve the remaining 15% of children presenting with these illnesses. These major referral hospitals also serve adjacent municipalities surrounding Guatemala City, which together constitute the Guatemalan metropolitan area. The proportion of children who reside in the surrounding metropolitan area and who develop serious infections resulting in referral to these hospitals is unknown. For this reason we calculated incidence rates only for children who lived in Guatemala City; the remaining analyses include all eligible children, regardless of residence. Based on projections from the 1994 census, the National Statistics Institute estimates that 326 779 children less than 5 years of age were living in the Guatemalan metropolitan area in 1997; of these, 121 003 were living in Guatemala City.

Case definitions

Children with possible invasive bacterial disease were identified by daily reviews of admission logbooks and laboratory results at each institution. Meningitis was defined as either a cerebrospinal fluid (CSF) white blood cell count (WBC) ≥ 10 cells/mm^3 or a positive bacterial culture or latex agglutination antigen test for Hib or *S. pneumoniae* in the CSF. Data were also analyzed using the World Health Organization (WHO) definition of probable meningitis: CSF protein > 100 mg/dL or glucose < 40 mg/dL or WBC > 100/mm^3 with > 80% neutrophils. Bacterial meningitis was confirmed by a positive bacterial CSF culture or latex agglutination antigen test for Hib or *S. pneumoniae* (14). A child was diagnosed as having pneumonia if he or she had fever, cough, tachypnea, and/or a chest radiograph showing infiltrates. Children with wheezing were excluded unless the chest radiograph revealed lobar consolidation; we did that because the primary purpose of this study was to identify children with bacterial disease. Confirmed bacterial pneumonia was defined as detection of any bacteria by blood or pleural fluid culture or a positive pleural fluid latex agglutination test for Hib or *S. pneumoniae*. The admitting physician diagnosed sepsis based on fever and signs of severe illness (e.g., toxic appearance and hypotension). A child with meningitis, pneumonia, and/or sepsis was classified as having a primary diagnosis of meningitis. A child with sepsis and pneumonia was classified as having pneumonia. Clinical signs of septic arthritis, epiglottitis, pericarditis, abscess, or cellulitis were used to define these other invasive bacterial diseases. For these illnesses, Hib or *S. pneumoniae* disease was diagnosed by culture from blood or other normally sterile fluid.

Laboratory procedures

A preliminary review of 365 CSF samples obtained in one of the hospitals in 1995 from children suspected of having meningitis revealed only one Hib isolate and one *S. pneumoniae* isolate. The chocolate agar used in the hospitals at that time was made from discarded human blood. This agar was demonstrated to be less sensitive than commercial chocolate agar supplemented with IsoVitaleX™ (Becton Dickinson Microbiology Systems, Cockeysville, Maryland, United States), based on serial dilution of a log phase growth of Hib. Prior to initiating surveillance, the laboratories began using supplemented commercial chocolate agar.

Blood cultures were obtained at the discretion of the admitting physicians. Blood was cultured in brain-heart infusion broth supplemented with sodium polyanethol sulfonate (SPS).

Subcultures on IsoVitaleX™-enriched chocolate agar and MacConkey agar were performed at 24 hours and, if turbidity developed, in the next 7 days. In May 1997, automated blood cultures for detection of bacterial growth (BACTEC, Becton Dickinson Microbiology Systems, Lutherville, Maryland, United States) were introduced at two of the hospitals; that was done at the third hospital in January 1998. Cerebrospinal fluid, pleural fluid, and fluid from other normally sterile sites were also cultured in broth and on IsoVitaleX™-enriched chocolate agar and MacConkey agar following standard procedures. *H. influenzae* isolates were confirmed as serotype b by detection of Hib antigen by latex agglutination (Directigen, Becton Dickinson Microbiology Systems, Lutherville, Maryland, United States) in the same body fluid or supernatant of broth cultures. Isolates with colony morphology consistent with *S. pneumoniae* were confirmed by optochin disk sensitivity. Aliquots of CSF, serum, pleural fluid, and other usually sterile fluids were stored at 2 °C to 8 °C and tested within 24 hours for Hib and *S. pneumoniae* antigens by latex agglutination. Prior to being tested, sera, pleural fluid, and joint fluid were heat-treated in accordance with the manufacturer's recommendations. Testing of sera was discontinued after the first year because of the limited added value and the high cost of the tests. Antigen testing for all other fluids was conducted throughout the surveillance period.

Statistical methods

Data were collected on standard forms, entered into a database using Epi Info version 6.0 software (Centers for Disease Control and Prevention, Atlanta, Georgia, United States), and analyzed using SPSS-PC version 10 software (SPSS, Inc., Chicago, Illinois, United States). Proportions were compared using two-tailed chi-square or Fisher's exact tests. Meningitis incidence rates for Guatemala City residents were estimated based on the city's projected population of children less than 5 years of age in 1997 and the assumption that 85% of Guatemala City children with meningitis were cared for at the three study hospitals.

Ethical reviews

The Committee on Human Research of the Bloomberg School of Public Health of Johns Hopkins University and the board for research and education at each hospital approved the study.

RESULTS

Of the 1 203 children studied, 1 080 (89.8%) had cultures of blood or usually sterile body fluids. Blood culture isolation rates were significantly improved ($P < 0.001$) following the introduction of the automated blood culture systems, from 6.3% (24/384) to 14.4% (72/501). Receipt of antibiotics prior to admission was reported for 563 (46.8%) of the children. Meningitis and pneumonia were the diseases most commonly associated with Hib and *S. pneumoniae* infections (Table 1). The highest incidence of Hib and *S. pneumoniae* was in the first 12 months of age, and 33.3% of Hib and 37.7% of *S. pneumoniae* occurred before 6 months of age (Figure 1).

Meningitis

Of the 357 children with meningitis, 87 of them (24.4%) also had pneumonia, 7 (2%) had sepsis, and 4 (1.1%) had both pneumonia and sepsis. Of the 357, 204 of them (57.1%) were male. Bacterial etiology was confirmed in 157 of the 357 children (44.0%), 146 by positive CSF culture or antigen test and 11 by a positive blood culture and inflammatory changes in the CSF. Of the 157 bacteriologically confirmed cases of meningitis, Hib was identified in 71 (45.2%) and *S. pneumoniae* in 46 (29.3%) (Table 1). Among these cases of bacterial meningitis, Directigen antigen detection identified 26 of the 71 cases of meningitis due to Hib (36.6%) and 10 of the 46 cases of *S. pneumoniae* meningitis (21.7%) not detected by CSF or blood cultures. Two false-positive CSF Hib latex agglutination tests were observed. In one of those tests a child had *S. aureus* isolated from CSF. In the other false-positive test a child had *S. aureus* bacteremia associated with a peripheral white blood cell count of 51 810 and the CSF culture had no growth; the

TABLE 1. Distribution of invasive diseases by etiology and diagnosis for children 1–59 months of age, Guatemala City, Guatemala, 1 October 1996–31 January 1999

Diagnosis	*Haemophilus influenzae*	*Streptococcus pneumoniae*	Other bacteria	No organisms found	Total cases with culture or latex agglutination	Total
Meningitis	71	46	40[a]	200	357	357
Pneumonia	24	30	34[b]	612	700	725
Sepsis	3	1	0	29	33	34
Cellulitis	6	0	1	49	56	60
Septic arthritis	1	0	2	6	9	9
Epiglottitis	2	0	0	1	3	3
Other	0	0	0	4	4	15
Total	107	77	77	901	1 162	1 203

[a] These 40 "other bacteria" were: *Neisseria meningitis* (7), *Salmonella* spp. (8), *Staphylococcus aureus* (8), *Escherichia coli* (4), *Pseudomonas aeruginosa* (5), and other organisms, including *Streptococcus* spp. and other enteric gram-negative bacteria (8).

[b] These 34 "other bacteria" were: *S. aureus* (21), *Streptococcus* spp. (6), *Salmonella* spp.(1), E. coli (1), *P. aeruginosa* (3), and other gram-negative bacteria (2).

FIGURE 1. Age distribution (percentage) of children 1–59 months of age hospitalized with *Haemophilus influenzae* type b or with *Streptococcus pneumoniae* in Guatemala City, Guatemala, 1 October 1996–31 January 1999

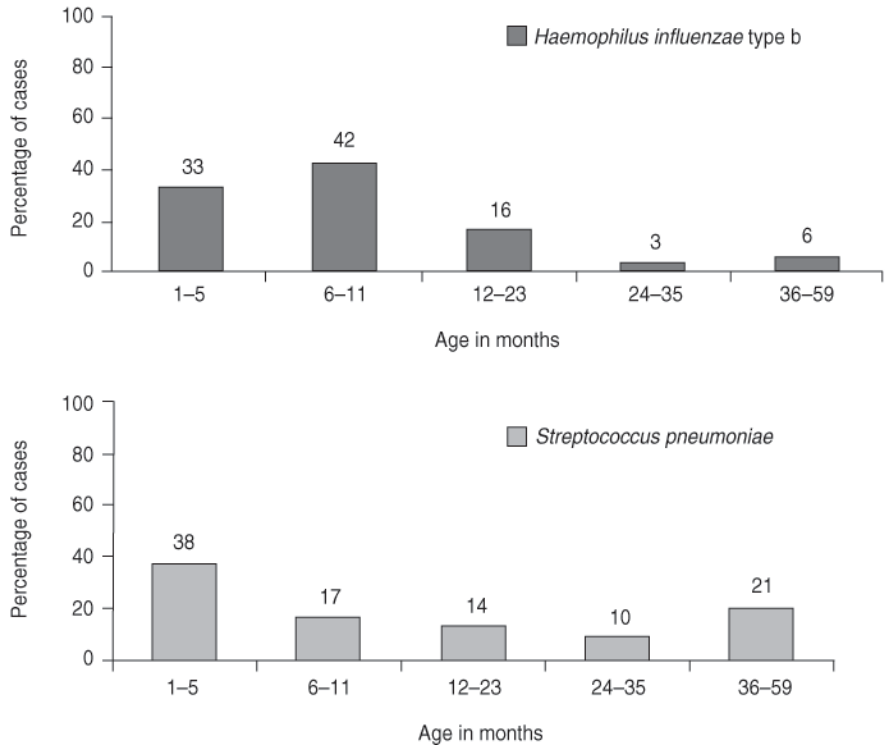
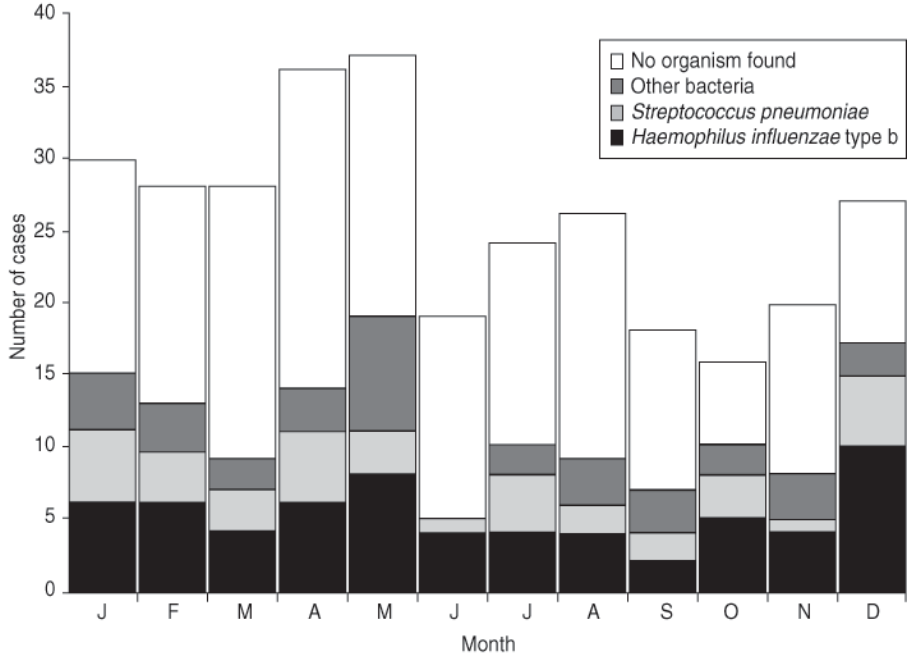


FIGURE 2. Seasonality of meningitis by etiology in children 1–59 months of age, Guatemala City, Guatemala, 1 October 1996–31 January 1999



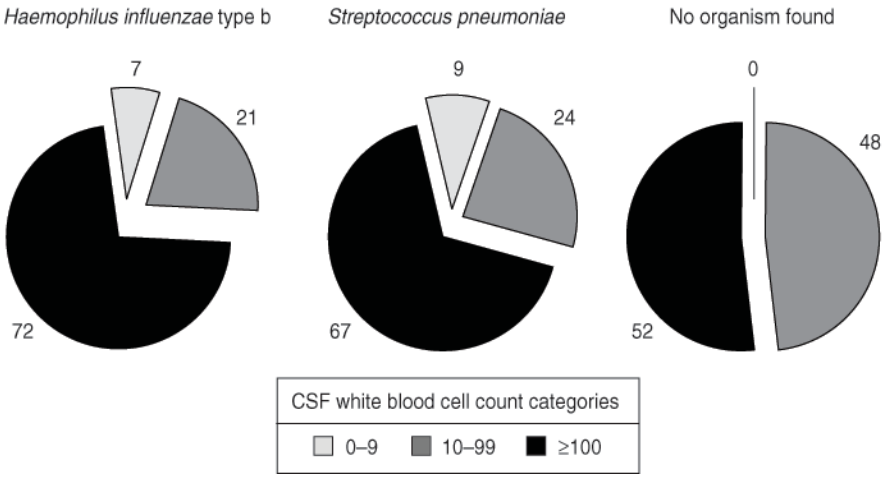
CSF white blood cell count was 389, with a glucose of 1 mg/dL, and protein of 155 mg/dL.

Antibiotic therapy before hospital admission was reported for 156 of the 357 children with meningitis (43.7%). Among the 37 children with Hib meningitis who received antibiotics before admission, 19 of them (51.4%) had a positive CSF or blood culture, while 26 of the 34 (76.5%) who had not received prior antibiotics had positive CSF cultures ($P = 0.05$). Similarly, among children with *S. pneumoniae* meningitis, 9 of the 16 children (56.3%) with prior antibiotic use had positive CSF cultures, but 27 of the 30 children (90.0%) with no prior antibiotics had positive CSF cultures ($P = 0.02$).

The average incidence rate for meningitis of any cause was 85.4 per 100 000 children/year among children under 5 years of age in Guatemala City; the rate for Hib meningitis was 13.8 per 100 000 and for *S. pneumoniae* meningitis, 11.7 per 100 000 children. Fifty-four percent of meningitis occurred prior to 6 months of age and 79.6% before 12 months of age. Of the 71 children with Hib meningitis, 23 of them (32.4%) were younger than 6 months of age, and 27 of the 46 children with *S. pneumoniae* meningitis (58.7%) were also less than 6 months of age. Of the 35 children with meningitis due to *Neisseria meningitidis, Salmonella* spp., *Escherichia coli, Pseudomonas* spp., and other enteric organisms, 22 of them (62.9%) had onset of disease between 1 and 6 months of age. The age distribution for children with no organism identified from CSF was similar to the age distribution for confirmed bacterial meningitis. A majority (59.4%) of children with meningitis presented during the dry season (December through May), but no seasonal pattern was observed for meningitis caused by Hib or *S. pneumoniae* (Figure 2).

The median CSF white blood cell count for children with bacterial meningitis was 330/mm^3. The CSF contained under 100 WBC/mm^3 in 28.6% of children with Hib and 32.6% of children with *S. pneumoniae* meningitis (Figure 3). Of the 71 children with Hib meningitis, 5 of them (7.0%) had

FIGURE 3. Distribution (percentage) of cerebrospinal fluid (CSF) white blood cell count by etiology in children 1–59 months of age with meningitis, Guatemala City, Guatemala, 1 October 1996–31 January 1999



under 10 WBC / mm^3 in the CSF; that was also true for 4 of the 46 children (8.7%) with *S. pneumoniae* meningitis. These 9 children with low CSF white cell counts had positive CSF latex agglutination tests for Hib or *S. pneumoniae.* Additionally, one of these 5 children with Hib and all 4 of the children with *S. pneumoniae* meningitis had the organism cultured from the CSF.

Of the 357 children with meningitis as defined by CSF > 10 WBC / mm^3 or positive culture or latex agglutination test, 280 of them (78.4%) met the WHO criteria for probable bacterial meningitis (> 100 WBC / mm^3 or protein > 100 mg / dL or glucose < 40 mg / dL). Of the 77 children who did not meet the WHO criteria, 9 (11.7%) had positive cultures or latex agglutination tests. Twenty-four additional children who had < 100 WBC / mm^3 in the CSF met the WHO criteria for probable bacterial meningitis based on CSF protein or glucose. None of these children had a positive blood or CSF culture or latex agglutination test.

The overall case fatality rate (CFR) for meningitis was 23.0% (Table 2). Children with *S. pneumoniae* meningitis had a higher CFR than children with Hib meningitis (37.0% vs. 14.1%, $P = 0.01$). Children with no organism identified by culture or antigen detection had a CFR of 18.0%. The CFR for children with meningitis and pneumonia was somewhat higher than the CFR for children with meningitis only (27.5% vs. 20.1%, $P = 0.19$). The CFR for the 37 children with Hib meningitis who resided outside Guatemala City was higher than the CFR for the children with Hib meningitis who lived within the city limits (24.3% vs. 3.0% respectively, $P < 0.02$).

Pneumonia

Seven hundred and twenty-five children had a primary diagnosis of pneumonia; 425 of them (58.6%) were male. Of the 725, 267 of them (36.8%) were under 6 months of age, and 204 of them (28.1%) were between 6 and 12 months of age. The median age for children with primary pneumonia was 8.1 months. A chest radiograph was obtained on 692 of the 725 children with pneumonia (95.4%); lobar or segmental consolidation was observed in 463 of the 692 (66.9%) and pleural effusions in 65 of the 692 (9.4%).

Just over one half (367 of 725, or 50.6%) of children with pneumonia received antibiotics before admission. Seven hundred of 725 (96.6%) children with pneumonia had blood or pleural fluid cultures or pleural fluid latex testing. Hib was identified in the blood or pleural fluid in 24 of 700 children (3.4%), and *S. pneumoniae* in 30 of the 700 (4.3%). An organism was identified by culture or latex agglutination in pleural fluid from 41 of 68 children (60.3%) with pleural effusion. One additional child with pleural effusion had *Staphylococcus aureus* isolated from the blood. Of the 68 children with pneumonia and pleural effusion, *S. pneumoniae* was identified in 28 of them (41.2%), *S. aureus* in 8 (11.8%), and Hib in 5 (7.4%).

The overall CFR was 8.0% (58 of 725) (Table 3) for children with a primary diagnosis of pneumonia and 10.1% (7 of 69) for children with pneumonia and pleural effusion.

Sepsis

Presumptive sepsis was diagnosed on admission in 164 children; 7 of these children also had meningitis, 119 also had pneumonia, and 4 also had meningitis and pneumonia. The median age was 5.3 months for children with presumptive sepsis, and 58.5% (96 of 164 were male. Of the 164 children, 24 children with presumptive

TABLE 2. Case fatality rate by etiology for children with meningitis, Guatemala City, Guatemala, 1 October 1996–31 January 1999

Etiology	No. of children studied	No. of deaths	Case fatality rate (%)
Haemophilus influenzae type[b]	71	10	14.1
Streptococcus pneumoniae	46	17	37.0
Other bacteria	40	19	47.5
No organisms found	200	36	18.0
Total	357	82	23.0

TABLE 3. Case fatality rate by diagnosis, Guatemala City, Guatemala, 1 October 1996–31 January 1999

Diagnosis	No. of children studied	No. of deaths	Case fatality rate (%)
Meningitis	357	82	23.0
Pneumonia	725	58	8.0
Sepsis	34	6	17.7
Cellulitis	60	0	0.0
Septic arthritis	9	1[a]	11.1
Epiglottitis	3	1	33.3
Other	15	1	6.7
Total	1 203	149	12.4

[a] This patient also had trauma.

sepsis (14.6%) had an organism isolated from blood. Thirty-four of the 164 (20.7%) children with presumptive sepsis were given the final diagnosis of sepsis, as no other focal infection was identified. Hib was identified in 3 of the 33 children (9.1%) with sepsis who had a blood culture, and *S. pneumoniae* in 1 child (3.0%).

DISCUSSION

The use of improved culture methods and latex agglutination antigen detection resulted in significantly increased rates of identification of Hib and *S. pneumoniae* as causes of bacterial invasive diseases in Guatemalan children. Other factors contributing to the prior underestimation of Hib and *S. pneumoniae* as important causes of severe disease include infrequently obtained blood cultures and high rates of antibiotic use prior to hospitalization. The estimated annual incidence of Hib and *S. pneumoniae* meningitis for children under 5 years of age in this population was lower than what has been observed in some other developing countries (4, 5, 15, 16). The true incidence is probably higher than 13.8 per 100 000, given the frequent use of antibiotics prior to hospitalization and the high CFR (18.0%) in children with negative CSF cultures and negative latex agglutination antigen detection tests. Other investigators have shown that prior antibiotic therapy was associated with decreased concentrations of bacteria in the CSF, and many children with culture-negative meningitis have evidence of a bacterial etiology (17, 18). In this study the likelihood of obtaining a positive culture for children with other evidence of Hib or *S. pneumoniae* meningitis was significantly lower for children who had reported prior antibiotic therapy than for untreated children.

The high CFRs for Hib meningitis and for *S. pneumoniae* meningitis were consistent with observations in other developing countries (4–8). The higher CFR for children with meningitis residing outside of Guatemala City was most likely due to delayed therapy and selective referral of children with more severe disease.

Although children with proven bacterial meningitis generally have high CSF white blood cell counts, using a cutoff point of > 100 WBC / mm^3 to define bacterial meningitis would have resulted in missing nine children with Hib or *S. pneumoniae* meningitis (14). None of the children with fewer than 100 WBC / mm^3 in the CSF who met the WHO criteria for possible meningitis based on elevated CSF protein or low glucose had evidence of bacterial etiology based on culture or latex agglutination testing of CSF. We believe that a simplified definition of $\geq$ 10 WBC / mm^3 is a better screening criterion for suspect meningitis.

In the 1980s, before the introduction of Hib conjugate vaccines in the United States and other countries where blood cultures were obtained more commonly, meningitis constituted approximately 50% of all invasive Hib disease (2, 4). However, meningitis constituted 66.4% of all invasive Hib disease diagnosed in Guatemalan children, most likely due to decreased detection of nonmeningitis Hib disease in children referred to hospitals.

The cases of pneumonia due to Hib and *S. pneumoniae* in this study are undoubtedly an underestimate of the true burden of disease due to these organisms because of the low use of blood cultures in children presenting with suspect pneumonia and the treatment of many children with pneumonia as outpatients. During the first year of the study we attempted to increase the identification of Hib and *S. pneumoniae* in children presenting with sepsis or pneumonia by testing sera using latex agglutination. Latex agglutination for testing heated sera or pleural fluid resulted in good sensitivity and specificity for detection of Hib in other studies (19–21). While we were able to identify several cases of Hib disease, the cost-effectiveness of this test is low.

Surveillance for target diseases is important to help understand the potential value of vaccines that are under consideration for introduction into immunization programs. Conjugate Hib and *S. pneumoniae* vaccines could prevent many of the serious infections resulting in hospitalization of Guatemalan children (6, 9, 13, 22–25). An evaluation of the potential impact of Hib conjugate vaccine is under way following the introduction of this vaccine in the Hospital General del Instituto Guatemalteco de Seguridad Social.

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RESUMEN

Meningitis y neumonía en niños guatemaltecos: importancia de *Haemophilus influenzae* tipo b y de *Streptococcus pneumoniae*

Objetivo. Determinar las características epidemiológicas de las infecciones invasoras por *Haemophilus influenzae* tipo b (Hib) y *Streptococcus pneumoniae* en niños hospitalizados en Guatemala. La importancia de este tema radica en que la vacunación contra Hib no ha sido incorporada a los programas de inmunización establecidos en Guatemala y en que los registros hospitalarios de 1995 indicaban una baja incidencia de meningitis e infecciones invasoras causadas por Hib y *S. pneumoniae*.

Métodos. Los niños hospitalizados en la Ciudad de Guatemala con signos clínicos de infección bacteriana se estudiaron en busca de indicios de infección por Hib o *S. pneumoniae*. Se cultivaron líquidos corporales normalmente estériles y se hicieron pruebas de detección de antígenos en líquidos cefalorraquídeo (LCR) y pleural.

Resultados. De los 1 203 niños de 1 a 59 meses de edad hospitalizados en un período de 28 meses, 725 (60,3%) tenían un diagnóstico primario de neumonía, 357 (29,7%) de meningitis, 60 (5,0%) de celulitis y 61 (5,1%) de sepsis u otras afecciones. En 20,0% de los niños con meningitis se detectó Hib y en 12,9% *S. pneumoniae*. La incidencia media anual de meningitis por Hib fue de 13,8 casos por 100 000 niños menores de 5 años de edad; 32,4% de los casos de meningitis causados por Hib y 58,7% de los causados por *S. pneumoniae* ocurrieron en niños menores de 6 meses de edad. La tasa de letalidad fue de 14,1%, 37,0% y 18,0%, respectivamente, para los casos de meningitis por Hib, por *S. pneumoniae* y con resultados negativos tanto en el cultivo como en las pruebas de detección de antígeno. El tratamiento previo con antibióticos fue frecuente y se vio asociado con una reducción significativa de resultados positivos en el cultivo de LCR en los niños que presentaban otros signos de meningitis por Hib o *S. pneumoniae*.

Conclusiones. El perfeccionamiento de la detección de casos, los métodos de cultivo y las pruebas de aglutinación con látex para la detección antigénica en LCR permitió identificar a Hib y *S. pneumoniae* como causas importantes de enfermedades graves en niños guatemaltecos. El empleo de un punto de corte de más de 10 leucocitos por milímetro cúbico de LCR mejoraría la sensibilidad de la detección de la meningitis bacteriana y ayudaría a calcular la carga de esta enfermedad en Guatemala y otros países en desarrollo.