Epidemiological surveillance study of *Streptococcus pneumoniae* in Latin America: Serotype distribution. A Pan American Health Organization initiative

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Streptococcus pneumoniae causes a variety of clinical conditions, including pneumonia, meningitis, bacteremia and otitis media. This micro-organism is the most common single bacterial agent responsible for respiratory tract infections. Each year, more than one million children are estimated to die each year from pneumococcal pneumonia, half of whom are infants younger than one year of age.

Current efforts to prevent mortality and morbidity due to pneumococcal infections in children are focused on early diagnosis and prompt antimicrobial therapy; however, the spread of antimicrobial resistance is leading to the research of new complementary strategies, such as vaccination. Unfortunately, the available 23-valent pneumococcal vaccine is not recommended for children younger than two years of age due to the vaccine's poor immunogenicity. The development of an adequate pneumococcal vaccine for a particular region will depend on the existence of detailed, reliable and representative data on the prevalence and serotype distribution of *S pneumoniae*. In Latin America, published data on this issue are scarce.

Recognizing this problem, the Pan American Health Organization, through its Special Program for Vaccines and Immunization and Sistema Regional de Vacunas, with major

funding from the Canadian International Development Agency, designed and implemented an intercountry and multi-institutional collaborative study in six Latin American countries.

The objectives of the collaborative study were to determine the prevalence of capsular types of *S pneumoniae* that cause invasive disease, particularly pneumonia, in children younger than five years of age; to monitor the patterns of susceptibility to penicillin and other antibiotics; to establish and strengthen regional laboratory facilities and epidemiological capabilities for monitoring capsular types, subtypes and antimicrobial susceptibility; and to create a bank of isolates that could be used for further research.

SUBJECTS AND METHODS

The study population included children younger than five years of age with invasive *S pneumoniae* isolated from a normally sterile site. Clinical diagnoses among the children included pneumonia (World Health Organization criteria), meningitis, sepsis, bacteremia, arthritis or peritonitis. Basic epidemiological information, including each child's sex, age, height and weight, and information regarding each child's

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TABLE 1

Number of *Streptococcus pneumoniae* isolates identified in Latin American countries

	Argentina	Brazil	Chile	Colombia	Mexico	Uruguay	Total
1993 to 1996	424	364	196	323	171	169	1647
1993 to 1997 (estimated)	800	800	400	500	300	300	3100

TABLE 2

Clinical diagnoses of invasive pneumococcal disease in Latin American children

	Pneumonia (%)	Meningitis (%)	Sepsis (%)	Other (%)
1993 to 1996	50.5	32.5	11.3	5.8
1993 to 1997 (estimated)	40	60	—	—

TABLE 3

Distribution of invasive *Streptococcus pneumoniae* capsular types from Latin American children (1993 to 1996) (n [%])

Type	Argentina	Brazil	Chile	Colombia	Mexico	Uruguay	Total
14	131 (31.0)	86 (23.6)	31 (15.7)	71 (22.0)	19 (11.1)	61 (38.6)	399 (24.4)
6B/6A	38 (9.0)	54 (14.9)	19 (9.6)	49 (15.2)	22 (13.0)	11 (7.0)	193 (11.8)
5	54 (12.8)	35 (9.6)	31 (15.7)	34 (10.5)	7 (4.1)	25 (15.8)	186 (11.4)
1	46 (10.9)	50 (13.7)	27 (13.6)	29 (9.0)	3 (1.8)	12 (7.6)	167 (10.2)
23F	9 (2.1)	13 (3.6)	7 (3.5)	31 (9.6)	28 (16.4)	5 (3.2)	93 (5.7)
19F	13 (3.6)	14 (3.8)	8 (4.0)	23 (7.1)	13 (7.6)	3 (1.9)	74 (4.5)
19a	13 (3.1)	13 (3.6)	13 (3.6)	3 (0.9)	13 (7.6)	7 (4.4)	62 (3.8)
17F	27 (6.4)	2 (0.5)	11 (5.6)	9 (2.8)	1 (0.6)	5 (3.2)	55 (3.4)
9V	15 (3.5)	19 (5.2)	3 (1.5)	4 (1.2)	4 (2.3)	5 (3.2)	50 (3.1)
18C	1 (0.2)	10 (2.7)	9 (4.5)	15 (4.6)	5 (2.9)	4 (2.5)	44 (2.7)
3	5 (1.2)	9 (2.5)	7 (3.5)	4 (1.2)	2 (1.2)	7 (4.4)	34 (2.1)
4	2 (0.5)	9 (2.5)	2 (1.0)	8 (2.5)	7 (4.1)	0 (0.0)	28 (1.7)
16F	12 (2.8)	2 (0.5)	1 (0.5)	2 (0.6)	1 (0.6)	0 (0.0)	18 (1.1)
9N	7 (1.7)	5 (1.4)	3 (1.5)	2 (0.6)	0 (0.0)	0 (0.0)	17 (1.0)
15B	1 (0.2)	2 (0.5)	1 (0.5)	6 (1.9)	4 (2.3)	1 (0.6)	15 (0.9)
Total	—	—	—	—	—	—	1649

TABLE 4

Percentage coverage of Latin American countries by proposed vaccine formula

Vaccine	Argentina	Brazil	Chile	Colombia	Mexico	Uruguay	All regions
7-valent	72	72.8	68.7	74.3	61.6	78.5	71.8
9-valent	81.9	78.5	75.8	78.3	64.5	84.9	78.3
12-valent	83.8	86.2	84.8	86.6	72.7	91.8	84.3

TABLE 5

Antimicrobial susceptibility: Diminished susceptibility to penicillin (DSP) by country and by *Streptococcus pneumoniae* serotype in Latin American countries (1993 to 1996)

	Argentina	Brazil	Chile	Colombia	Mexico	Uruguay	All regions
DSP (%)	24	22	30	16	47	33	28
Serotype (%)							
23F	0	0	10	46	61	0	—
14	60	48	23	32	8	89	—

health, including the clinical presentation of their pneumococcal disease, previous antibiotic use and outcome of illness, were collected.

Six Latin American countries participated in the study – Argentina, Brazil, Chile, Colombia, Mexico and Uruguay. The se-

lection of countries was based on epidemiological criteria and operational feasibility.

Isolates were confirmed as *S pneumoniae* by standard methods; all isolates were preserved at -70°C and lyophilized. Isolates were typed by capsular reaction test (Quellung test)

with a 12-pool system (Danish nomenclature). All isolates were screened for penicillin susceptibility, using oxacillin disks (1 µg). Minimal inhibitory concentrations for penicillin G, ceftriaxone, trimethoprim/sulfamethoxazole, chloramphenicol and erythromycin were also determined. Inhibition zones and minimal inhibitory concentrations were interpreted according to guidelines of the National Committee for Clinical Laboratory Standards, Villanova, Pennsylvania. For quality assurance purposes, a panel of five unknowns were submitted, periodically, by the National Centre for Streptococcus (NCS), Edmonton, Alberta, the international reference centre for the study, to the national reference laboratories in each country. At the same time, the laboratories submitted 10% of their isolates to the NCS.

The sample size for the study was calculated to find a serotype with a prevalence of 5%, with an absolute precision of 2% and a 95% CI.

RESULTS

Table 1 reveals the number of *S pneumoniae* isolates identified in each of the participating countries. The total number of isolates identified between 1993 and 1996 was 1647. The most common form of invasive pneumococcal disease identified was pneumonia, followed by meningitis (Table 2).

A number of different capsular types were identified throughout the participating Latin American countries (Table 3). There was some variation in the prominence of serotypes by country. Serotype 14 was the most common type isolated in all countries excluding Mexico. Based on the distribution of capsular types, three hypothetical vaccine formulae – a 7-valent vaccine, a 9-valent vaccine and a 12-valent vaccine – were evaluated to determine the optimal number of capsular types that should be included in a vaccine designed to provide children with protection against *S pneumoniae* across the study region. The proportion of invasive *S pneumoniae* infections caused by isolates included in the three proposed vaccines in all regions combined ranged from 71.8% to 84.3% (Table 4).

Antimicrobial susceptibility of the isolates was monitored (Table 5). The proportion of isolates with diminished susceptibility to penicillin (DSP) varied by country, from a low of 16% in Colombia to a high of 47% in Mexico. In all regions combined, 28% of isolates had DSP. In Colombia and Mexico, 46% to 61% of isolates with DSP belonged to capsular type 23F; however, in Uruguay, Argentina and Brazil, 48% to 89% of isolates with DSP were serotype 14.

DISCUSSION

A number of goals have been achieved with this collaborative study. *S pneumoniae* serotypes that need to be included in a vaccine targeted for children in the study region have been identified. As well, studies designed to assess the impact of observed antibiotic resistance on clinical outcome have been implemented. Training and technology transfer associated with the use of molecular methods to characterize *S pneumoniae* further has taken place, and linkages have been en-

hanced among the national public health laboratories in the study region. An organized quality assurance system has been established, as has a national surveillance program in each of the participating countries.

In the future, it is anticipated that the networks created during this study will be maintained and reinforced. It is also expected that the networks will expand to involve other countries. Cuba has participated since 1997, and professionals from Peru, Dominican Republic and Guatemala have been trained recently in laboratory procedures. In 1998, two workshops were presented to standardize laboratory procedures – one with participants from all Central American countries and the other with members of the remaining South American countries. It is hoped that future studies will be implemented to establish the relevance of antimicrobial resistance, the disease incidence and risk factors, and the evaluation of new diagnostic methods. Additionally, it has been decided to give high priority to the surveillance of invasive infections caused by *Haemophilus influenzae* type b and *Neisseria meningitidis*. This activity is essential for the evaluation, implementation and monitoring of the effectiveness of vaccination programs.

PARTICIPATING LATIN AMERICAN INSTITUTIONS: División de Laboratorios de Salud Pública, Montevideo, Uruguay; Instituto Nacional de Salud Pública, Cuernavaca, Mexico; Instituto Nacional de Salud, Santa Fe de Bogotá, Colombia; Instituto de Salud Pública, Santiago de Chile, Chile; Instituto Adolfo Lutz, Sao Paulo, Brazil; Ministerio de Asistencia Social y Salud Pública de la Nación, Buenos Aires, Argentina

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