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Serotype Distribution and Antimicrobial Resistance of *Streptococcus pneumoniae* Isolated in Algiers, Algeria

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There are few data on antibiotic resistance of *Streptococcus pneumoniae* in Algeria. Among 309 strains, 34.6% were penicillin G-nonsusceptible *S. pneumoniae* strains (25.2% were intermediate and 9.4% were resistant). Serotypes 1, 5, 14, and 6 were the most frequent in invasive child infections. A multicenter study to standardize the national guidelines is needed.

Acute lower respiratory tract infections and diarrheal diseases are still the most common causes of death of children in developing countries (8). In Algeria, in 1998, the morbidity rates for acute lower respiratory tract infections and diarrheal diseases from admitted children were 15 and 14.7%, while the mortality rates were 26 and 16%, respectively (18a).

Streptococcus pneumoniae is the leading cause of pneumonia and the second cause of acute otitis media (AOM) and meningitis in Algeria (15, 19). Despite its importance, little information on the antimicrobial resistance of this bacterium is known. The only preliminary report in the eastern part of the country showed that 12.5% were penicillin G-nonsusceptible *S. pneumoniae* (PNSSP) (24).

Resistance rates are usually higher in children, and variations in the distribution of the resistance between regions and countries are well known (1, 7, 13, 21).

In order to assess the rates of drug resistance and serotype distribution of pneumococci, especially in children, a study was conducted from January 1996 to October 2000.

This work was presented, in part, at the 38th Interscience Conference on Antimicrobial Agents and Chemotherapy in San Diego, Calif. (N. Ramdani-Bouguessa, R. Denine, and K. Rahal, Abstr. 38th Intersci. Conf. Antimicrob. Agents Chemother., abstr. E-15, 1998).

A total of 309 consecutive strains were collected: 215 were from Béni-Messous hospital and 94 were from five health centers located in Algiers, Algeria. All isolates were sent to the Algeria Pasteur Institute for susceptibility testing and storage. Isolates were identified by alpha-hemolysis, susceptibility to optochin, and bile solubility. Strains were frozen first at −20 until 1998 and then −70°C.

Susceptibility to erythromycin, tetracycline, chloramphenicol, co-trimoxazole, rifampin, and vancomycin (Sanofi Diagnostic Pasteur, Marnes-la-Coquette, France) was determined by the disk diffusion method. MICs were determined by agar dilution method for penicillin and by Etest (AB Biodisk, Solna, Sweden) for amoxicillin and cefotaxime. A 0.5 McFarland solution was used to inoculate a Mueller-Hinton agar plate containing 5% sheep blood, incubated at 35°C in a CO_2 atmosphere. The ATCC 49619 and ATCC 49619 strains of *S. pneumoniae* were used as quality control. The breakpoints were those recommended by the NCCLS (17).

Serotyping was first realized by latex agglutination at the Centre de Référence des Pneumocoques, Créteil, France (P. Geslin), and by Quellung reaction (5) in our laboratory dating back to 2000, using antisera from the Statens Serum Institute (Copenhagen, Denmark) kindly offered by the United Nations International Children's Emergency Fund. Factor sera to distinguish types within groups were not available.

Among the 309 isolates, 240 came from children (77.6%); 169 (70.2%) of these were from children under 5 years of age.

The MICs at which 50 and 90% of the isolates tested were inhibited were, respectively, 0.032 and 2 mg/liter for penicillin (range, 0.016 to 4 mg/liter), 0.016 and 1 mg/liter for amoxicillin (range, 0.016 to 4 mg/liter), and 0.016 and 0.5 mg/liter for cefotaxime (range, 0.016 to 2 mg/liter).

Among invasive strains, no high resistance to amoxicillin and cefotaxime was found, while five strains among the noninvasive ones showed the highest resistance level to penicillin (4 mg/liter), amoxicillin (4 mg/liter), and cefotaxime (2 mg/liter); one strain was isolated from AOM and four from bronchial aspirate, almost all tested in patients with a chronic lung condition (Table 1).

Resistance to other drugs was as follows: 26.4% for tetracycline, 25.7% for co-trimoxazole, 21.7% for erythromycin, and 4.6% for chloramphenicol. No resistance was observed for rifampin and vancomycin. Multiple resistance, i.e., resistance to three or more groups of antibiotics, was observed in 146 (47.2%) strains, all with reduced susceptibilities to penicillin G.

Due to several failures in the storage conditions, only 258 of 309 strains were viable for serotyping (Table 2). Among the 115 invasive serotyped strains, serotypes 1 and 5 were the most frequent in both adults and children. In 10 cases (50%), serotype 1 was isolated from children 5 years of age and over, while among children under 5 years old, the most frequent types were, in decreasing order, serotypes 5, 1, 3, 14, and 6, which together comprised 60% of pediatric strains. Serotype 14 was almost exclusively isolated from cerebrospinal fluid (CSF) in children under 2 years of age.

Sixty-eight (86%) of 79 PNSSP strains belonged to five se-

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TABLE 1. Penicillin, amoxicillin, and cefotaxime susceptibilities

Isolate type and source of isolate	No. of isolates	No. of isolates that are intermediate (I) or resistant (R) to:					
		Penicillin G		Amoxicillin		Cefotaxime	
		I (%)	R (%)	I (%)	R (%)	I (%)	R (%)
Invasive							
CSF	54	9 (16.6)	6 (11.1)	0	0	4 (7.4)	0
Blood	45	2 (4.4)	1 (1.8)	0	0	1 (1.8)	0
Pleural fluid	18	3 (16.6)	0	0	0	0	0
Other[a]	6	0	0	0	0	0	0
All	123	14 (11.4)	7 (5.7)	0	0	5 (4)	0
Noninvasive							
Middle ear	97	24 (24.7)	4 (4.1)	1 (1)	0	2 (2)	0
Other[b]	48	17 (35.4)	5 (10.4)	0	0	4 (8.3)	0
Lower respiratory[c]	41	13 (31.7)	13 (31.7)	4 (9.7)	0	7 (17)	3 (7.3)
All	186	64 (34.4)	22 (11.8)	5 (2.7)	0	13 (7)	3 (1.6)

[a] Ascitic fluid, joint fluid, and pericardic fluid.
[b] Genital, skin, and eye.
[c] Fibroscopic aspirate and sputum.

rotypes or serogroups: 23, 14, 6, 19, and 9. High resistance to penicillin G was seen in serogroups 23, 14, and 6.

This study is the first complete regional one that has been conducted in Algeria. These results highlight the rare isolation of pneumococci because of limited laboratory facilities. Furthermore, most infections are often empirically treated and the small number of pneumococci isolated from children suffering from pneumonia is explained by the low rate of positive blood cultures in 10 to 20% (2).

Our results show that Algeria is classified among the regions with high rates of drug resistance in pneumococci (>10%) (1).

Although data are scarce, several studies conducted in developing countries showed that pneumococcus resistance rates vary from region to region. In North and West Africa, the prevalence of PNSSP is 53.7% in Tunisia (S. Ben Redjeb, J. Boukadida, A. Hammani, A. Kamoun, F. Mahjoubi, O. Boullegue, A. Kechrid, and C. H. Jribi, Abstr. 38th Intersci. Conf. Antimicrob. Agents Chemother., abstr. E-11, 1998), 9% in Morocco, and 61.7 and 22.4% in Senegal and the Ivory Coast, respectively (3).

The findings of Tunisia's study are comparable to our results, although the rates of PNSSP in CSF are higher than those isolated in Algeria. By contrast, in Uganda a high rate of PNSSP, 83.5%, is reported (11).

In Asian countries, the prevalence of PNSSP from invasive infections in children was 1.3% in India (10) and 12.7% in

TABLE 2. Serotype distribution of most frequent serotype of *S. pneumoniae* strains isolated from invasive and noninvasive infections in children and adults (n = 258)

Serotype	Total no. of isolates	No. of isolates that cause:							
		Invasive infections					Noninvasive infections		
		Total	Meningitis		Pleuropneumonia		Total	Children	Adults
			Children	Adults	Children	Adults			
1	38	33	5	3	11	12	5	5	
3	22	8	4			2	14	11	3
5	16	12	5		3	4	4	4	
6	27	6	2		1	2	21	19	2
7	8	6	3	1	1	1	2	2	
9	9	4	2		1	1	5	5	
10	6	4		1	1	2	2	1	1
11	7	4	1	1	1	1	3	2	1
12	4	3	2		1		1	1	
13	4	1			1		3	3	
14	21	6	6				15	15	
16	4	3	1			2	1	1	
18	8	2	1		1		6	6	
19	23	4	1	1	1	1	19	17	2
23	26	6	3	1		1	20	20	
24	4	2	1		1		2	1	1
35	7	1	1				6	5	1
Other[a]	24	10	3		1	2	14	10	4

[a] Other serotypes: 2 (n = 2), 4 (n = 2), 15 (n = 3), 20 (n = 2), 21 (n = 1), 28 (n = 1), 33 (n = 2), 34 (n = 4), 37 (n = 2), 38 (n = 1), 43 (n = 1), and not typeable (n = 3).

Bangladesh (20). The rate was 24.9% in Latin American countries (12). Spain, Hungary, and South Africa have the highest rates in the world (6, 7, 16).

In this study, rates of co-trimoxazole resistance are relatively low compared to those found in African and Asian countries (3, 9, 11, 25). This may be explained by the fact that antibiotics are not delivered without prescription and that co-trimoxazole is used as the second line of defense in treating bacterial acute lower respiratory tract infections after amoxicillin failure. One of the acute respiratory tract infection national program objectives is to reduce unnecessary antibiotic use; efforts in educational training are being realized.

Rates of PNSSP are higher in CSF, cefotaxime, or ceftriaxone; a dose of 300 mg/kg of body weight is required for empirical treatment with or without vancomycin, depending on MICs (14, 18). On the other hand, amoxicillin is effective for the treatment of pneumonia and AOM.

Serotype distribution is according to the data published in developing countries, where serotypes 1 and 5 are the most prevalent (22, 24, 25).

One of the most significant findings from this study is the infrequency of serogroups 19 and 23 in invasive isolates in contrast to their frequency in noninvasive isolates in children. Serotypes 19F and 23F are known to be poorly immunogenic in children under 5 years (4).

Our preliminary results from the molecular PNSSP study lead to a clonal diffusion of resistance. Clusters are detected on PNSSP with penicillin G MICs that are $\geq$0.25 mg/liter, the serotype 23F intercontinental clone was found, and the clusters of serotype 6B and 14, except one 6B cluster, are closely related to the French clones (unpublished data). In the absence of financial resources, this study could not be finished.

The continuous monitoring of pneumococcus drug resistance is needed to assess the real issues regarding drug resistance; this will allow doctors to adjust the empirical treatment. Because of serotype coverage, variations by region, and the cost of pneumococcal conjugate vaccines (10, 23), the judicious use of antibiotics is critical in preventing the increase of pneumococcus drug resistance in developing countries.

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